10789106.trn

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT

MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:44:07 ON 01 MAR 2007

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:44:22 ON 01 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 FEB 2007 HIGHEST RN 923894-67-1
DICTIONARY FILE UPDATES: 28 FEB 2007 HIGHEST RN 923894-67-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

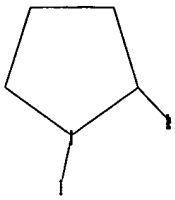
Please note that search-term pricing does apply when conducting SmartSELECT searches.

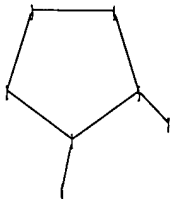
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

10789106.trn

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10789106.str



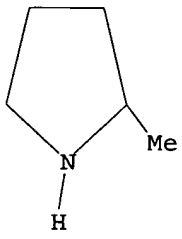


chain nodes :
6 7
ring nodes :
1 2 3 4 5
chain bonds :
1-6 5-7
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5
exact bonds :
1-6 2-3 3-4 4-5 5-7
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:44:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 42265 TO ITERATE

4.7% PROCESSED 2000 ITERATIONS 5 ANSWERS

```
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       833023 TO   857577
PROJECTED ANSWERS:            1497 TO     2729

L2            5 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:44:42 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   847724 TO ITERATE

100.0% PROCESSED   847724 ITERATIONS                          3292 ANSWERS
SEARCH TIME: 00.00.04

L3         3292 SEA SSS FUL L1

=> FIL HCAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   172.10     172.31

FILE 'HCAPLUS' ENTERED AT 11:44:52 ON 01 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 1 Mar 2007  VOL 146 ISS 10
FILE LAST UPDATED: 28 Feb 2007  (20070228/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l3
L4         2322 L3

=> s l4 and process for preparing
       2386179 PROCESS
       1622071 PROCESSES
       3561269 PROCESS
                  (PROCESS OR PROCESSES)
         58858 PREPARING
             2 PREPARINGS
         58859 PREPARING
                  (PREPARING OR PREPARINGS)
```

```
        135459 PREPG
            12 PREPGS
        135470 PREPG
                 (PREPG OR PREPGS)
        170366 PREPARING
                 (PREPARING OR PREPG)
         23129 PROCESS FOR PREPARING
                 (PROCESS(1W)PREPARING)
L5           19 L4 AND PROCESS FOR PREPARING

=> s l5 and iodide
        181560 IODIDE
         24970 IODIDES
        191672 IODIDE
                 (IODIDE OR IODIDES)
L6            4 L5 AND IODIDE

=> s l4 and process
       2386179 PROCESS
       1622071 PROCESSES
       3561269 PROCESS
                 (PROCESS OR PROCESSES)
L7          149 L4 AND PROCESS

=> s l7 and iodide
        181560 IODIDE
         24970 IODIDES
        191672 IODIDE
                 (IODIDE OR IODIDES)
L8           13 L7 AND IODIDE

=> s l8 and hydrogenating
          8565 HYDROGENATING
L9            0 L8 AND HYDROGENATING

=> s l8 and hydrogenation
        175196 HYDROGENATION
          2288 HYDROGENATIONS
        175433 HYDROGENATION
                 (HYDROGENATION OR HYDROGENATIONS)
L10           1 L8 AND HYDROGENATION

=> FIL REGISTRY
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               26.00     198.31

FILE 'REGISTRY' ENTERED AT 11:50:57 ON 01 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 FEB 2007  HIGHEST RN 923894-67-1
DICTIONARY FILE UPDATES:  28 FEB 2007  HIGHEST RN 923894-67-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.
```

10789106.trn

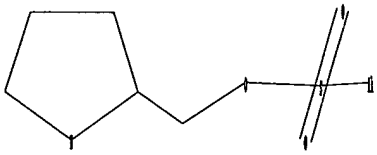
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

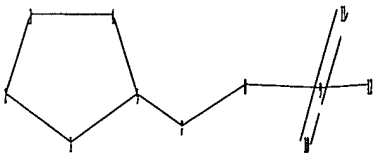
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10789106a.str



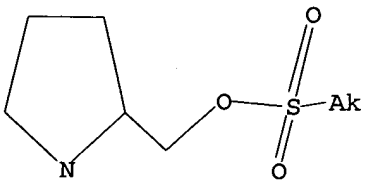


chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5
chain bonds :
5-7 7-8 8-9 9-10 9-11 9-12
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 7-8 8-9 9-10 9-11 9-12
exact bonds :
2-3 3-4 4-5 5-7
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS

L11 STRUCTURE UPLOADED

=> d l11
L11 HAS NO ANSWERS
L11 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l11
SAMPLE SEARCH INITIATED 11:51:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       38 TO ITERATE

100.0% PROCESSED       38 ITERATIONS                                 7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          391 TO     1129
PROJECTED ANSWERS:               7 TO      298

L12           7 SEA SSS SAM L11

=> s l11 sss full
FULL SEARCH INITIATED 11:51:37 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      915 TO ITERATE

100.0% PROCESSED      915 ITERATIONS                               277 ANSWERS
SEARCH TIME: 00.00.01

L13         277 SEA SSS FUL L11

=> FIL HCAPLUS
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.10     370.41

FILE 'HCAPLUS' ENTERED AT 11:51:44 ON 01 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 1 Mar 2007  VOL 146 ISS 10
FILE LAST UPDATED: 28 Feb 2007  (20070228/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l13
L14           223 L13

=> s l14 and iodide
        181560 IODIDE
         24970 IODIDES
```

```
        191672 IODIDE
                 (IODIDE OR IODIDES)
L15          27 L14 AND IODIDE

=> s l14 and alkali metal iodide
        410332 ALKALI
          6988 ALKALIS
         32121 ALKALIES
        432922 ALKALI
                 (ALKALI OR ALKALIS OR ALKALIES)
       1716890 METAL
        865791 METALS
       2083823 METAL
                 (METAL OR METALS)
        181560 IODIDE
         24970 IODIDES
        191672 IODIDE
                 (IODIDE OR IODIDES)
          1362 ALKALI METAL IODIDE
                 (ALKALI(W)METAL(W)IODIDE)
L16           0 L14 AND ALKALI METAL IODIDE

=> s l15 and metal
       1716890 METAL
        865791 METALS
       2083823 METAL
                 (METAL OR METALS)
L17           1 L15 AND METAL

=> s l15 and alkali
        410332 ALKALI
          6988 ALKALIS
         32121 ALKALIES
        432922 ALKALI
                 (ALKALI OR ALKALIS OR ALKALIES)
L18           0 L15 AND ALKALI

=> d his

     (FILE 'HOME' ENTERED AT 11:44:07 ON 01 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 11:44:22 ON 01 MAR 2007
L1               STRUCTURE UPLOADED
L2             5 S L1
L3          3292 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 11:44:52 ON 01 MAR 2007
L4          2322 S L3
L5            19 S L4 AND PROCESS FOR PREPARING
L6             4 S L5 AND IODIDE
L7           149 S L4 AND PROCESS
L8            13 S L7 AND IODIDE
L9             0 S L8 AND HYDROGENATING
L10            1 S L8 AND HYDROGENATION

     FILE 'REGISTRY' ENTERED AT 11:50:57 ON 01 MAR 2007
L11              STRUCTURE UPLOADED
L12            7 S L11
L13          277 S L11 SSS FULL
```

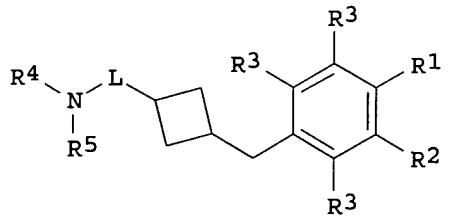
```
     FILE 'HCAPLUS' ENTERED AT 11:51:44 ON 01 MAR 2007
L14          223 S L13
L15           27 S L14 AND IODIDE
L16            0 S L14 AND ALKALI METAL IODIDE
L17            1 S L15 AND METAL
L18            0 S L15 AND ALKALI

=> s l15 and hydrogenating
          8565 HYDROGENATING
L19          0 L15 AND HYDROGENATING

=> s l15 and hydrogenation
        175196 HYDROGENATION
          2288 HYDROGENATIONS
        175433 HYDROGENATION
                (HYDROGENATION OR HYDROGENATIONS)
L20          0 L15 AND HYDROGENATION

=> s l15 and hydroge
            65 HYDROGE
             2 HYDROGES
            67 HYDROGE
                (HYDROGE OR HYDROGES)
L21          0 L15 AND HYDROGE

=> d his

     (FILE 'HOME' ENTERED AT 11:44:07 ON 01 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 11:44:22 ON 01 MAR 2007
L1               STRUCTURE UPLOADED
L2             5 S L1
L3          3292 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 11:44:52 ON 01 MAR 2007
L4          2322 S L3
L5            19 S L4 AND PROCESS FOR PREPARING
L6             4 S L5 AND IODIDE
L7           149 S L4 AND PROCESS
L8            13 S L7 AND IODIDE
L9             0 S L8 AND HYDROGENATING
L10            1 S L8 AND HYDROGENATION

     FILE 'REGISTRY' ENTERED AT 11:50:57 ON 01 MAR 2007
L11              STRUCTURE UPLOADED
L12            7 S L11
L13          277 S L11 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 11:51:44 ON 01 MAR 2007
L14          223 S L13
L15           27 S L14 AND IODIDE
L16            0 S L14 AND ALKALI METAL IODIDE
L17            1 S L15 AND METAL
L18            0 S L15 AND ALKALI
L19            0 S L15 AND HYDROGENATING
L20            0 S L15 AND HYDROGENATION
L21            0 S L15 AND HYDROGE

=> d l5 ibib abs hitstr tot
```

L5 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1312595 HCAPLUS
DOCUMENT NUMBER: 146:62583
TITLE: Cyclobutyl amine derivatives and their preparation, pharmaceutical compositions and use as histamine-3 receptor ligands
INVENTOR(S): Liu, Huaqing; Hancock, Arthur A.; Cowart, Marlon D.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 87pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

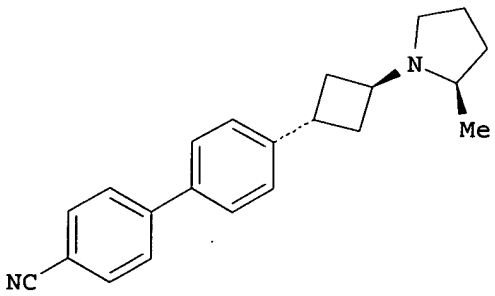
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006132914	A2	20061214	WO 2006-US21257	20060601

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-687357P P 20050603
OTHER SOURCE(S): MARPAT 146:62583
GI



I

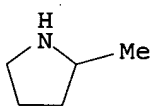


II

AB Compds. of formula I are useful in treating conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Also disclosed are pharmaceutical compns. comprising the histamine-3 receptor ligands, methods for using such compds. and compns., and a process for preparing compds. within the scope of formula I. Compds. of formula I wherein R1 and R2 are independently H, alkyl, alkoxy, halo, CN, thioalkoxy, ether, acyl, etc.; each R3 are independently H, alkyl, alkoxy, halo, CN and thioalkoxy; R4 and R5 are independently (fluoro)alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, etc.; and their pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, are claimed. Example compound II was prepared by reduction of 3-(4-bromophenyl)cyclobutanone; the resulting 3-(4-bromophenyl)-cis-cyclobutanol underwent condensation with (R)-2-methylpyrrolidine to give 1-[3-(4-bromophenyl)-trans-cyclobutyl]-(2R)-2-methylpyrrolidine, which underwent cross-coupling with 4-cyanophenylboronic acid to give compound II. All the invention compds. were evaluated for their histamine-3 receptor binding affinity.

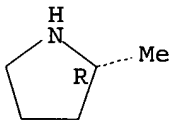
IT 765-38-8, 2-Methylpyrrolidine 41720-98-3
59335-84-1, (S)-2-Methylpyrrolidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclobutyl amine derivs. useful in therapy of diseases)

RN 765-38-8 HCAPLUS
CN Pyrrolidine, 2-methyl- (CA INDEX NAME)



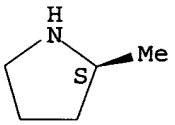
RN 41720-98-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 59335-84-1 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1033644 HCAPLUS
DOCUMENT NUMBER: 145:397503

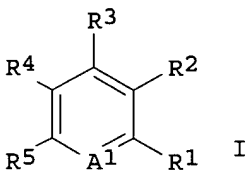
TITLE: Preparation of oxazole and thiazole derivatives as H3-receptor ligands with numerous therapeutic uses
INVENTOR(S): Celanire, Sylvain; Denonne, Frederic
PATENT ASSIGNEE(S): Ucb S.A., Belg.
SOURCE: PCT Int. Appl., 200pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006103045	A1	20061005	WO 2006-EP2806	20060328
WO 2006103045	B1	20061130		

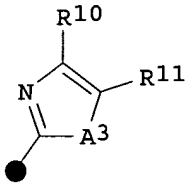
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2005-6971 A 20050331
OTHER SOURCE(S): MARPAT 145:397503
GI



I



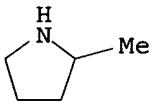
II

AB The present invention relates to compds. comprising an oxazole or thiazole moiety (shown as I; variables defined below; e.g. 1-[3-[4-[4-[(2-methylpyrrolidin-1-yl)methyl]-1,3-oxazol-2-yl]phenoxy]propyl]piperidine (1)), processes for preparing them (synthetic intermediates but no methods of preparation are claimed), pharmaceutical compns. comprising said compds. and their uses (no data) as H3-receptor ligands. For I: A1 is CH, C(alkyl), C-halogen or N; R1 is H, halogen, C1-6 alkyl or alkoxy; R2 is II; A3 is O or S; R3 is H, halogen, C1-6 alkyl or alkoxy; R4 is H, halogen, C1-6 alkyl, alkoxy or -O-L; R5 is H or -O-L, wherein L is an aminoalkyl group and at least one of R4 and R5 should be -O-L; R10 and R11 = H, sulfonyl, amino, et al.; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for >100 examples of I are included. For example, 1 was prepared (42 %) at room temperature by mixing 4-(chloromethyl)-2-[4-(3-chloropropoxy)phenyl]-1,3-oxazole (preparation given), NaI, K2CO3, and 2-methylpyrrolidine in MeCN for 72 h, after which piperidine was added and the mixture stirred at 80° overnight. In an [35S]GTPγS-binding assay using human histamine H3-receptor, compds.

I showed pIC50 6.5-10. In a paced isolated guinea pig myenteric plexus - elec.-field stimulation assay for antagonism activity, compds. I showed pA2 values typically ≥6.5 for the histamine H3 receptor.

IT 765-38-8, 2-Methylpyrrolidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxazole and thiazole derivs. as histamine H3-receptor ligands with numerous therapeutic uses)

RN 765-38-8 HCAPLUS
CN Pyrrolidine, 2-methyl- (CA INDEX NAME)



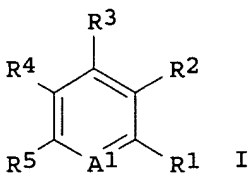
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1033643 HCAPLUS
DOCUMENT NUMBER: 145:397502
TITLE: Preparation of oxazoline and thiazoline derivatives as histamine H3-receptor ligands with numerous therapeutic uses
INVENTOR(S): Celanire, Sylvain; Talaga, Patrice; Leurs, Regorius; Denonne, Frederic; Timmerman, Henkdrik; Lebon, Florence
PATENT ASSIGNEE(S): Ucb S.A., Belg.
SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

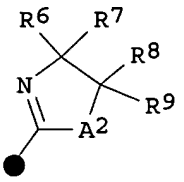
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006103057	A1	20061005	WO 2006-EP2860	20060329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2005-6971 A 20050331
OTHER SOURCE(S): MARPAT 145:397502
GI



I



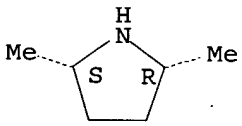
II

AB The present invention relates to compds. comprising an oxazoline or thiazoline moiety (shown as I; variables defined below; e.g. 1-[3-[4-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)phenoxy]propyl]piperidine (1)), processes for prepg . them (synthetic intermediates but no methods of preparation are claimed), pharmaceutical compns. comprising said compds. and their uses (no data) as H3-receptor ligands. For I: A1 is CH, CMe or N; R1 is H or halogen; R2 is II; A2 is O or S; R3 is H, halogen, C1-4 alkyl or C1-4 alkoxy; R4 is H, halogen, C1-4 alkyl, C1-4 alkoxy, trifluoromethyl or -O(CH2)nNR12aR12b each CH2 in -O(CH2)nNR12aR12b being (un)substituted by one or two C1-4 alkyl; R5 is H or -O(CH2)mNR13aR13b, each CH2 in -O(CH2)mNR13aR13b being (un)substituted by one or two C1-4 alkyl, and at least one of R4 and R5 should be a -O(CH2)nNR12a/13aR12b/13b group; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for >30 examples of I are included. For example, 1 was prepared in 5 steps (80, 99, 95, 97 and 83 %) starting from 4-benzyloxybenzoic acid and 2-amino-2-methylpropan-1-ol to give 4-(benzyloxy)-N-(2-hydroxy-1,1-dimethylethyl)benzamide, with subsequent formation of the following intermediates: 2-[4-(benzyloxy)phenyl]-4,4-dimethyl-4,5-dihydro-1,3-oxazole, 4-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)phenol and 2-[4-(3-chloropropoxy)phenyl]-4,4-dimethyl-4,5-dihydro-1,3-oxazole. In an [35S]GTPγS-binding assay using human histamine H3-receptor, compds. I showed pIC50 6.5-10. In a paced isolated guinea pig myenteric plexus - elec.-field stimulation assay for antagonism activity, compds. I showed pA2 values typically ≥6.5 for the histamine H3 receptor.

IT 39713-71-8, cis-2,5-Dimethylpyrrolidine 135324-85-5, (2R)-2-Methylpyrrolidine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxazoline and thiazoline derivs. as histamine H3-receptor ligands with numerous therapeutic uses)

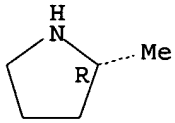
RN 39713-71-8 HCAPLUS
CN Pyrrolidine, 2,5-dimethyl-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 135324-85-5 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



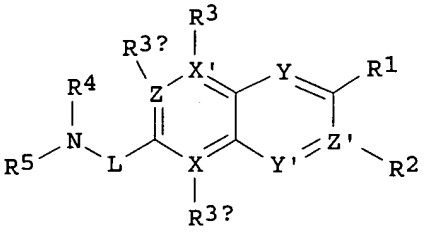
● HCl

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1294007 HCAPLUS
DOCUMENT NUMBER: 144:36332
TITLE: Preparation of tri-and bi-cyclic heteroaryl histamine-3 receptor ligands
INVENTOR(S): Altenbach, Robert J.; Black, Lawrence A.; Chang, Sou-Jen; Cowart, Marlon D.; Faghih, Ramin; Gfesser, Gregory A.; Ku, Yi-Yin; Liu, Huaqing; Lukin, Kirill A.; Nersesian, Diana L.; Pu, Yu-Ming; Curtis, Michael P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005272736	A1	20051208	US 2005-123324		20050506
PRIORITY APPLN. INFO.:			US 2004-570397P	P	20040512

OTHER SOURCE(S): MARPAT 144:36332
GI



I

AB Title compds. I [Y and Y' independently = CH, CF, and N; X, X', Z and W independently = C or N; one of R1 and R2 is selected from L2R6 with the other of R1 and R2 = H, alkyl, alkoxy, etc.; L2 = O, CO, S, NH, etc.; R6 = bicyclic or tricyclic ring, each containing at least two heteroatoms; R3 = H, alkyl, alkoxy, halo, etc., or R3 is absent when X' = N; R3a = H, Me, alkoxy, halo, etc., or R3a is absent when Z = N; R3b = H, OH, alkyl, alkoxy, etc., or R3b is absent when X = N; R4 and R5 independently = alkyl, haloalkyl, hydroxyalkyl, etc.; or R4 and R5 taken together to form

heterocyclic ring], and their pharmaceutically acceptable salts, are prepared and disclosed as useful in treating conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Also disclosed are pharmaceutical compns. comprising the histamine-3 receptor ligands, methods for using such compds. and compns., and a process for preparing I. Thus, e.g., 6-[2-((2R)-2-methylpyrrolidin-1-yl)ethyl]-2-(4H-thieno[3,2-b]pyrrol-5-yl)quinoline was prepared via a multistep synthesis from (S)-Toluene-4-sulfonic acid 5-oxopyrrolidin-2-ylmethyl ester. In histamine-3 receptor binding studies, I demonstrated binding affinities from 810 nM to 0.02 nM.

IT 69498-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tri-and bi-cyclic heteroaryl histamine-3 receptor ligands)

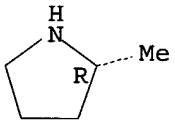
RN 69498-23-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

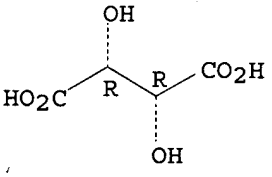
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



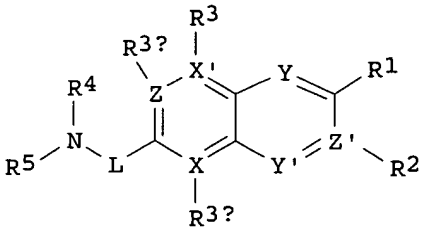
L5 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1293779 HCAPLUS
DOCUMENT NUMBER: 144:36264
TITLE: Preparation of bicyclic amines bearing heterocyclic substituents as H3 receptor ligands
INVENTOR(S): Altenbach, Robert J.; Black, Lawrence A.; Chang, Sou-Jen; Cowart, Marlon D.; Faghih, Ramin; Gfesser, Gregory A.; Ku, Yi-Yin; Liu, Huaqing; Lukin, Kirill A.; Nersesian, Diana L.; Pu, Yu-Ming; Curtis, Michael P.
PATENT ASSIGNEE(S): Abbott Laboratories, USA

10789106.trn

SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005272728	A1	20051208	US 2005-123620	20050506
US 7098222	B2	20060829		
PRIORITY APPLN. INFO.:			US 2004-570186P P	20040512
OTHER SOURCE(S):	MARPAT 144:36264			

GI



I

AB Title compds. I [Y, Y' = CH, CF, N; X, X', Z, Z' = C, N; R1, R2 = H, alkyl, alkoxy, aryl, cycloalkyl, etc.; R3 = absent when X' is N or H, alkyl, alkoxy, etc.; R3 = absent when X' is N or R3 = H, alkyl, alkoxy, halo, etc.; R3a = absent when Z is N or R3a = H, Me, alkoxy, halo, CN; R3b = absent when X is N or R3b = H, alkyl, alkoxy, halo, etc.; R4-5 = alkyl, haloalkyl, hydroxyalkyl, etc.; L = divalent alkyl, etc.] are prepared For instance, 6-[2-((2R)-2-methylpyrrolidin-1-yl)ethyl]-2-(4-methyl-2-thien-2-yl-1,3-thiazol-5-yl)quinoline is prepared in 7 steps from (S)-(5-oxopyrrolidin-2-yl)methyl 4-methylbenzenesulfonate, 1-(2-bromoethyl)-4-nitrobenzene, trimethylacetyl chloride, DMF and 1-(4-methyl-2-(thiophene-2-yl)thiazol-5-yl)ethanone. Representative compds. of the invention demonstrated binding affinities for the H3 receptor from about 810 nM to about 0.02 nM. I are useful for the treatment of conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Also disclosed are pharmaceutical compns. comprising the histamine-3 receptor ligands, methods for using such compds. and compns., and a process for preparing I.

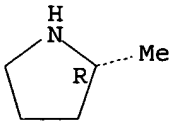
IT 69498-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic amines bearing heterocyclic substituents as H3 receptor ligands)

RN 69498-23-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

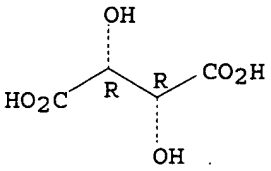
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1224283 HCAPLUS
DOCUMENT NUMBER: 143:477959
TITLE: Preparation of tri-and bi-cyclic heteroaryl histamine-3 receptor ligands
INVENTOR(S): Altenbach, Robert J.; Black, Lawrence A.; Chang, Sou-Jen; Cowart, Marlon D.; Faghih, Ramin; Gfesser, Gregory A.; Ku, Yi-Yin; Liu, Huaqing; Lukin, Kirill A.; Nersesian, Diana L.; Pu, Yu-Ming; Curtis, Michael P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005256309	A1	20051117	US 2004-844101	20040512
CA 2566898	A1	20051201	CA 2005-2566898	20050429
WO 2005113536	A2	20051201	WO 2005-US14866	20050429
WO 2005113536	A3	20060330		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1751130 A2 20070214 EP 2005-763655 20050429

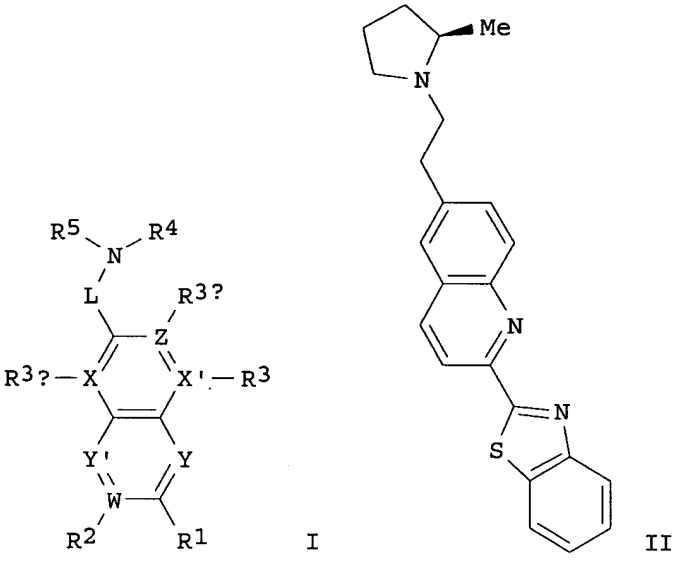
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2004-844101 A 20040512

WO 2005-US14866 W 20050429

OTHER SOURCE(S): CASREACT 143:477959; MARPAT 143:477959

GI



I II

AB Title compds. I [Y and Y' independently = CH, CF, and N; X, X', Z and W independently = C or N; one of R1 and R2 is selected from L2R6 with the other of R1 and R2 = H, alkyl, alkoxy, etc.; L2 = O, CO, S, NH, etc.; R6 = bicyclic or tricyclic ring, each containing at least two heteroatoms; R3 = H, alkyl, alkoxy, halo, etc., or R3 is absent when X' = N; R3a = H, Me, alkoxy, halo, etc., or R3a is absent when Z = N; R3b = H, OH, alkyl, alkoxy, etc., or R3b is absent when X = N; R4 and R5 independently = alkyl, haloalkyl, hydroxyalkyl, etc.; or R4 and R5 taken together to form heterocyclic ring], and their pharmaceutically acceptable salts, are prepared and disclosed as useful in treating conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Thus, e.g., II was prepared via a multistep synthesis from (S)-Toluene-4-sulfonic acid 5-oxopyrrolidin-2-ylmethyl ester. In histamine-3 receptor binding studies, I demonstrated binding affinities from 810 nM to 0.02 nM. Also disclosed are pharmaceutical compns. comprising the histamine-3 receptor ligands, methods for using such compds. and compns., and a process for preparing compds. within the scope of formula (I).

IT 135324-85-5

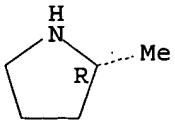
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tri-and bi-cyclic heteroaryl histamine-3 receptor ligands)

RN 135324-85-5 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



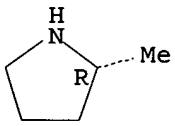
● HCl

IT 69498-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tri-and bi-cyclic heteroaryl histamine-3 receptor ligands)
RN 69498-23-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

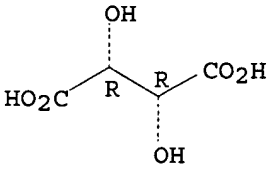
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



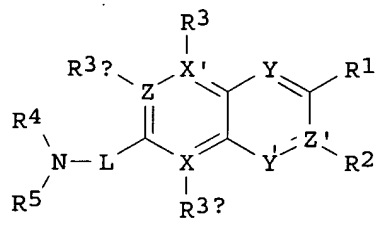
L5 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1223810 HCAPLUS
DOCUMENT NUMBER: 143:477862
TITLE: Preparation of bicyclic amines bearing heterocyclic substituents as H3 receptor ligands
INVENTOR(S): Altenbach, Robert J.; Black, Lawrence A.; Chang, Sou-Jen; Cowart, Marlon D.; Faghih, Ramin; Gfesser, Gregory A.; Ku, Yi-Yin; Liu, Huaqing; Lukin, Kirill A.; Nersesian, Diana E.; Pu, Yu-Ming; Curtis, Michael P.

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

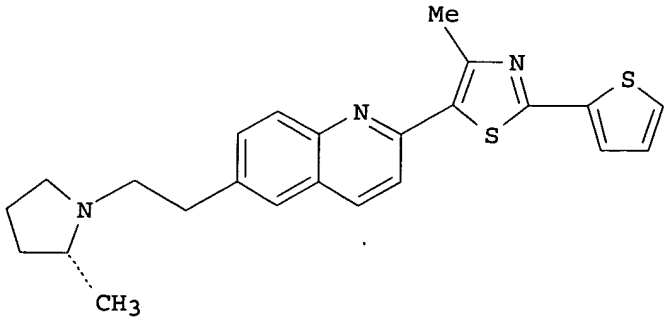
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005256118	A1	20051117	US 2004-843742	20040512
CA 2566896	A1	20051201	CA 2005-2566896	20050429
WO 2005113551	A1	20051201	WO 2005-US14863	20050429
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1751149	A1	20070214	EP 2005-743943	20050429
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-843742 A 20040512
WO 2005-US14863 W 20050429

OTHER SOURCE(S): CASREACT 143:477862; MARPAT 143:477862
GI



I



II

AB Title compds. I [Y, Y' = CH, CF, N; X, X', Z, Z' = C, N; R1, R2 = H, alkyl, alkoxy, aryl, cycloalkyl, etc.; R3 = absent when X' is N or H, alkyl, alkoxy, etc.; R3b = absent when Z is N or H, alkyl, alkoxy, halo, etc.; R4-5 = alkyl, haloalkyl, hydroxyalkyl, etc.; L = divalent alkyl, etc.] are prepared For instance, II is prepared in 7 steps from (S)-(5-oxopyrrolidin-2-yl)methyl 4-methylbenzenesulfonate, 1-(2-bromoethyl)-4-nitrobenzene, trimethylacetyl chloride, DMF and 1-(4-methyl-2-(thiophene-2-yl)thiazol-5-yl)ethanone. Representative compds. of the invention demonstrated binding affinities for the H3 receptor from about 810 nM to about 0.02 nM. I are useful for the treatment of conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Also disclosed are pharmaceutical compns. comprising the histamine-3 receptor ligands, methods for using such compds. and compns., and a process for preparing compds. within the scope of formula (I).

IT 69498-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic amines bearing heterocyclic substituents as H3 receptor ligands)

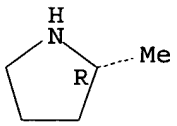
RN 69498-23-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

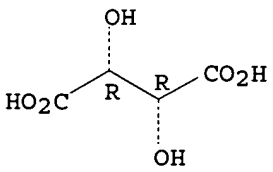
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



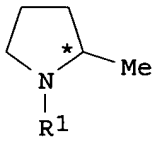
L5 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127154 HCAPLUS
DOCUMENT NUMBER: 142:74442
TITLE: Process for preparing

2-methylpyrrolidine and specific enantiomers thereof

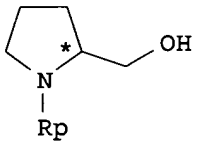
INVENTOR(S): Ku, Yi-Yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004260100	A1	20041223	US 2004-789106		20040227
PRIORITY APPLN. INFO.:			US 2003-450480P	P	20030227

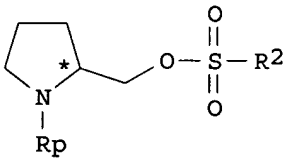
OTHER SOURCE(S): MARPAT 142:74442
GI



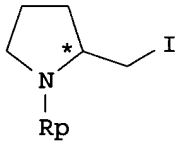
I



II



III



IV

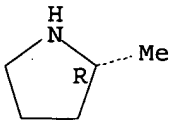
AB The invention relates to a process for preparing 2-methylpyrrolidine or N-protected 2-methylpyrrolidine (I) (R1 = H, a nitrogen-protecting group; * denotes an asym. carbon atom) and, more particularly, specific enantiomers of I. The compound I is useful as an intermediate to obtain a compound useful for modulating a histamine-3 receptor. Novel intermediates also such as N-protected prolinol (II) (Rp = a nitrogen-protecting group) and their sulfonate ester (III) [Rp = same as above; R2 = each (un)substituted alkyl or aryl], and 2-iodomethylpyrrolidine (IV) (Rp = same as above) are described. Thus, N-protection of (S)-prolinol by di-tert-Bu dicarbonate followed by esterification with methanesulfonyl chloride gave (S)-2-[(methanesulfonyloxy)methyl]pyrrolidine-1-carboxylic acid tert-Bu ester which was iodinated by NaI to give (S)-2-iodomethylpyrrolidine-1-carboxylic acid tert-Bu ester (V). Hydrogenolysis of V over 10% Pd-C gave (R)-2-methylpyrrolidine-1-carboxylic acid tert-Bu ester which was treated with HCl in EtOAc to give (R)-2-methylpyrrolidine hydrochloride.

IT 135324-85-5P, (R)-2-Methylpyrrolidine monohydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine, specific enantiomers thereof, and their intermediates from prolinol)

RN 135324-85-5 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



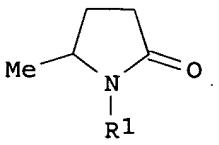
● HCl

L5 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:802619 HCAPLUS
DOCUMENT NUMBER: 141:295857
TITLE: Production of 5-methyl-N-aryl-2-pyrrolidone and 5-methyl-N-alkyl-2-pyrrolidone by reductive amination of levulinic acid esters with aryl and alkyl amines
INVENTOR(S): Manzer, Leo Ernest
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

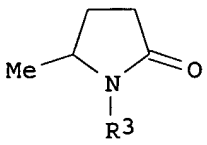
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192938	A1	20040930	US 2003-396219	20030324
AU 2004223846	A1	20041007	AU 2004-223846	20040323
CA 2520304	A1	20041007	CA 2004-2520304	20040323
WO 2004085348	A2	20041007	WO 2004-US9003	20040323
WO 2004085348	A3	20041118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1605756	A2	20051221	EP 2004-758118	20040323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009012	A	20060328	BR 2004-9012	20040323
CN 1764379	A	20060426	CN 2004-80008274	20040323
JP 2006521391	T	20060921	JP 2006-509255	20040323
US 2005033062	A1	20050210	US 2004-943313	20040917
US 2005033063	A1	20050210	US 2004-943315	20040917
US 2005038265	A1	20050217	US 2004-943327	20040917
US 2005137406	A1	20050623	US 2005-51706	20050204
US 7129362	B2	20061031		

PRIORITY APPLN. INFO.: US 2003-396219 A 20030324
WO 2004-US9003 W 20040323
OTHER SOURCE(S): CASREACT 141:295857; MARPAT 141:295857

GI



I



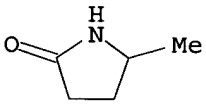
II

AB This invention relates to a process for producing 5-methyl-N-aryl-2-pyrrolidone, 5-methyl-N-alkyl-2-pyrrolidone, and 5-methyl-N-cycloalkyl-2-pyrrolidone [I, II; R1 = C6-30 aromatic group; R2 = each (un)substituted hydrocarbyl, C1-18 alkyl, alkenyl, cycloalkyl, or cycloalkyl containing at least one heteroatom, aryl, or heteroaryl; R3 = fully or partially reduced derivative of R1] by reductive amination of levulinic acid esters with aryl or alkyl amines utilizing a transition metal catalyst, which is optionally supported. Also disclosed is a process for preparing a pharmaceutical composition, a agrochem. composition, a cleaning composition, an ink jet composition, or a refrigerant or air conditioning lubricant containing the II. Thus, to a 5 mL pressure vessel was added 50 g 5% pt/C, and 1 g of a solution containing 30 weight% Et levulinate, 25 weight% 2-ethylaniline and 45 weight% dioxane. The vessel was sealed, charged with 5.52 MPa H, and heated to 150° for 4 h to give 5-methyl-N-(2-Ethylphenyl)-2-pyrrolidone with 49.1% selectivity and 95.3% conversion of Et levulinate.

IT 108-27-0P, 5-Methyl-2-pyrrolidone
RL: SPN (Synthetic preparation); PREP (Preparation)
(production of 5-methyl-N-aryl-2-pyrrolidone and 5-methyl-N-alkyl-2-pyrrolidone by reductive amination of levulinic acid esters with arylamines and alkylamines in presence of transition metal catalyst)

RN 108-27-0 HCAPLUS

CN 2-Pyrrolidinone, 5-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:802616 HCAPLUS

DOCUMENT NUMBER: 141:314148

TITLE: Production of 5-methyl-N-(arylmethyl)-2-pyrrolidone, 5-methyl-N-(cycloalkylmethyl)-2-pyrrolidone and 5-methyl-N-alkyl-2-pyrrolidone by reductive amination of levulinic acid esters with cyano compounds

INVENTOR(S): Manzer, Leo Ernest

PATENT ASSIGNEE(S): E. I. Du Pont De Nemours and Company, USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

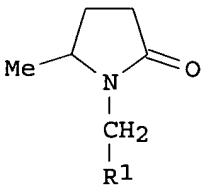
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192935	A1	20040930	US 2003-396087	20030324
US 6916842	B2	20050712		
AU 2004224292	A1	20041007	AU 2004-224292	20040323
CA 2520428	A1	20041007	CA 2004-2520428	20040323
WO 2004085048	A2	20041007	WO 2004-US8999	20040323
WO 2004085048	A3	20050901		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1606046	A2	20051221	EP 2004-758114	20040323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009040	A	20060328	BR 2004-9040	20040323
CN 1764638	A	20060426	CN 2004-80008243	20040323
JP 2006524683	T	20061102	JP 2006-507534	20040323
US 2005049423	A1	20050303	US 2004-966398	20041015
US 6930126	B2	20050816		
US 2005059829	A1	20050317	US 2004-966087	20041015
US 7025819	B2	20060411		
US 2005120912	A1	20050609	US 2004-966123	20041015
US 7014697	B2	20060321		
US 2005120913	A1	20050609	US 2004-966131	20041015
US 7030074	B2	20060418		

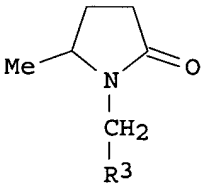
PRIORITY APPLN. INFO.: US 2003-396087 A 20030324
WO 2004-US8999 W 20040323

OTHER SOURCE(S): CASREACT 141:314148; MARPAT 141:314148

GI



I



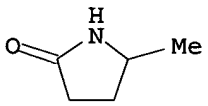
II

AB This invention relates to a process for producing 5-methyl-N-(arylmethyl)-2-pyrrolidone, 5-methyl-N-(cycloalkylmethyl)-2-pyrrolidone and 5-methyl-N-alkyl-2-pyrrolidone (I, II; R1 = C6-30 aromatic group; R3 = a fully or partially reduced derivative of R1) by reductive amination of levulinic acid esters with aryl or alkyl cyano compds. of formula R1-CN (R1 = same as above) utilizing a transition metal catalyst, which is optionally supported. Also disclosed is an process for preparing a pharmaceutical composition, an agrochem. composition, a cleaning composition, an ink jet composition, and a refrigerant or air conditioning lubricant containing the compound II. Thus, to a 5 mL pressure vessel was added 50 mg 5%

Ru/C, and 1 g of a solution containing 30 weight% Et levulinate, 22 weight% adiponitrile and 48 weight% dioxane. The vessel was sealed, charged with 5.52 MPa H, and heated to 150° for 4 h to give hexane-1,6-bis(5-methyl-N-alkyl-2-pyrrolidone) with 21.7% selectivity and 92.2% conversion of Et levulinate.

IT 108-27-0P, 5-Methyl-2-pyrrolidone
RL: SPN (Synthetic preparation); PREP (Preparation)
(production of methyl-N-(arylmethyl)pyrrolidone, methyl-N-(cycloalkylmethyl)pyrrolidone and methyl-N-alkylpyrrolidone by reductive amination of Et levulinate with cyano compds. in presence of transition metal catalyst)

RN 108-27-0 HCAPLUS
CN 2-Pyrrolidinone, 5-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:802615 HCAPLUS
DOCUMENT NUMBER: 141:295854
TITLE: Production of 5-methyl-1-hydrocarbyl-2-pyrrolidone by reductive amination of levulinic acid
INVENTOR(S): Manzer, Leo Ernest; Herkes, Frank E.
PATENT ASSIGNEE(S): E. I. Du Pont De Nemours and Company, USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

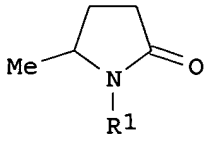
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192933	A1	20040930	US 2003-396046	20030324
US 6900337	B2	20050531		
AU 2004223847	A1	20041007	AU 2004-223847	20040323
CA 2520242	A1	20041007	CA 2004-2520242	20040323
WO 2004085349	A2	20041007	WO 2004-US9004	20040323
WO 2004085349	A3	20060504		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1613573	A2	20060111	EP 2004-758119	20040323

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

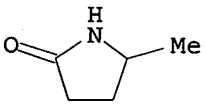
BR 2004009015 A 20060328 BR 2004-9015 20040323
PRIORITY APPLN. INFO.: US 2003-396046 A 20030324
WO 2004-US9004 W 20040323
OTHER SOURCE(S): CASREACT 141:295854; MARPAT 141:295854
GI



I

AB This invention relates to a process for producing 5-methyl-1-hydrocarbyl-2-pyrrolidone or 5-methyl-2-pyrrolidone (I; R1 = H, each (un)substituted C1-30 hydrocarbyl, C1-30 C1-C30 alkyl, C1-30 alkenyl, C1-30 alkynyl, C3-30 cycloalkyl, or C3-30 cycloalkyl containing at least one heteroatom), by reductive amination of levulinic acid with ammonia or primary amine of formula R1-NH2 (R1 = same as above) utilizing a transition metal catalyst, which may be optionally supported. Also disclosed is a process for preparing a pharmaceutical composition, an agrochem. composition, a cleaning composition, an ink jet composition, and a refrigerant or air conditioning lubricant containing the compound I (R1 = group listed above excluding H). Thus, a feedstock containing 20% ammonium levulinate, 40% octylamine, and 40% water, by weight was hydrogenated over pt/Calsicat C at a temperature and pressure of 150° and 6.9 Mpa, resp., for 18 h to give 99.0% 5-methyl-1-octyl-2-pyrrolidone, i.e. I (R1 = octyl).

IT 108-27-0P, 5-Methyl-2-Pyrrolidone
RL: SPN (Synthetic preparation); PREP (Preparation)
(production of 5-methyl-1-hydrocarbyl-2-pyrrolidone or 5-methyl-2-pyrrolidone by reductive amination of levulinic acid with ammonia or primary amine in presence of transition metal catalyst)
RN 108-27-0 HCAPLUS
CN 2-Pyrrolidinone, 5-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



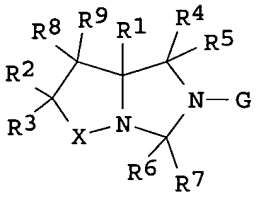
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:759871 HCAPLUS
DOCUMENT NUMBER: 141:277621
TITLE: Preparation of bicyclic compounds as modulators of androgen receptor function
INVENTOR(S): Sun, Chong-Qing; Hamann, Lawrence; Augeri, David; Bi, Yingzhi; Robl, Jeffrey; Huang, Yan-Ting; Wang, Tammy; Holubec, Alexandra; Simpkins, Ligaya; Sutton, James C.; Li, James J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 94 pp., Cont.-in-part of U.S.

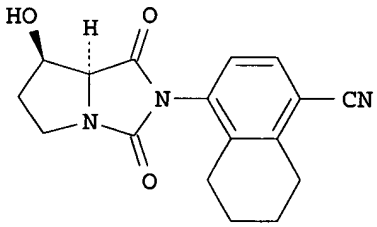
Pat. Appl. 2004 19,063.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004181064	A1	20040916	US 2004-780415		20040217
US 2004019063	A1	20040129	US 2003-438722		20030515
PRIORITY APPLN. INFO.:			US 2002-381616P	P	20020517
			US 2002-406711P	P	20020829
			US 2003-438722	A2	20030515

OTHER SOURCE(S): MARPAT 141:277621
GI



I



II

AB Bicyclic compds. of formula I [R1 = H, alkyl, arylalkyl, etc.; R2, R3 = H, alkyl, (substituted) OH, halo, (substituted) NH2, etc.; R4-R7 = H, alkyl, cycloalkyl, arylalkyl, aryl, etc.; R4R5, R6R7 = O, S, NH, CH2, etc.; R8, R9 = H, alkyl, (substituted) OH, (substituted) NH2, etc.; X = (CH2)n; n = 1-2] are prepared as modulators of androgen receptor function. Further provided are methods of using such compds. for the treatment of nuclear hormone receptor-associated conditions, such as age related diseases, for example sarcopenia. Also provided are pharmaceutical compns. containing such compds. and processes for preparing some of the compds. of the invention. Thus, II was prepared from 4-isocyanato-5,6,7,8-tetrahydronaphthalene-1-carbonitrile and Me (2S,3R)-3-hydroxy-2-pyrrolidinecarboxylate (prepns. given).

IT 627531-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic compds. as modulators of androgen receptor function)

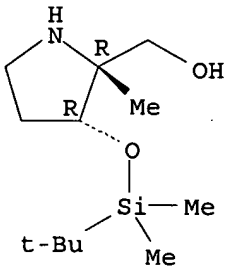
RN 627531-74-2 HCAPLUS

CN 2-Pyrrolidinemethanol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-, (2R,3R)-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

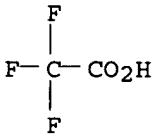
CRN 627531-73-1
CMF C12 H27 N O2 Si

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L5 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:722955 HCAPLUS
DOCUMENT NUMBER: 141:243334
TITLE: An efficient and cost-effective process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol
INVENTOR(S): Ku, Yi-yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171845	A1	20040902	US 2003-376534	20030227
CA 2515801	A1	20040910	CA 2004-2515801	20040225
WO 2004076388	A2	20040910	WO 2004-US5573	20040225
WO 2004076388	A3	20041202		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1601650	A2	20051207	EP 2004-714598	20040225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

JP 2006519233 T 20060824 JP 2006-503863 20040225
PRIORITY APPLN. INFO.: US 2003-376534 A 20030227
WO 2004-US5573 W 20040225

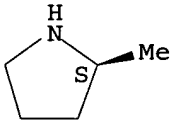
OTHER SOURCE(S): MARPAT 141:243334

AB The invention relates to an efficient and cost-effective process for preparing 2-methylpyrrolidine and, more particularly, specific enantiomers of 2-methylpyrrolidine, from (R/S)-prolinol. Novel intermediates also are described. The title compds. were synthesized in several steps via N-protection of corresponding chiral prolinols, conversion of the hydroxy groups to sulfonates or iodides, reduction and finally N-deprotection. The iodides could also be prepared from the corresponding sulfonates via reaction with metal iodides. Thus, (S)-prolinol was N-protected with tert-butoxycarbonyl anhydride (100% yield) followed by sulfonylation with mesyl chloride (96% yield). The resulting mesylate was either directly reduced to (R)-N-Boc-2-methylpyrrolidine with lithium triethoxyborohydride (54% yield) or via the iodide intermediate through iodination with LiI (79% yield) followed by hydrogenolysis in the presence of Pd/C (85.9% yield). (R)-N-Boc-2-methylpyrrolidine was then deprotected with HCl to give 2-(R)-methylpyrrolidine hydrochloride (96% yield).

IT 59335-84-1P, 2-(S)-Methylpyrrolidine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

RN 59335-84-1 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)- (9CI) (CA INDEX NAME)

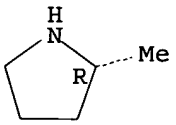
Absolute stereochemistry. Rotation (+).



IT 41720-98-3P, 2-(R)-Methylpyrrolidine 135324-85-5P, (R)-2-Methylpyrrolidine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target product; process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

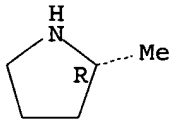
RN 41720-98-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 135324-85-5 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

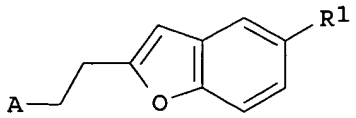


● HCl

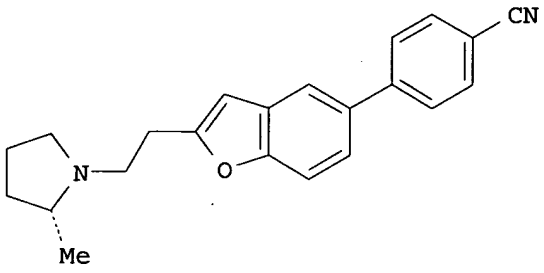
L5 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:252496 HCAPLUS
DOCUMENT NUMBER: 140:287256
TITLE: Process for preparing amine-substituted benzofurans
INVENTOR(S): Ku, Yi-yin; Pu, Yu-ming; Cowart, Marlon D.; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004024707	A2	20040325	WO 2003-US28396		20030910
WO 2004024707	A3	20040812			
W: CA, JP, MX					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
US 2004133007	A1	20040708	US 2003-654897		20030905
US 6822101	B2	20041123			
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	A	20020916
			US 2003-654897	A	20030905
			US 2002-411210P	P	20020916

OTHER SOURCE(S): CASREACT 140:287256; MARPAT 140:287256
GI



I



II

AB The present invention relates to processes for preparing amine substituted benzofurans, e.g. I [A = (substituted)pyrrolidinyl or (substituted)piperidinyl; R1 = (substituted)4-cyanophenyl, (substituted)aryl, (substituted)heteroaryl], and more particularly 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-1-benzofuran-5-yl)benzonitrile (II), were prepared via halogenation, cyclization, sulfonation, alkylation, and cross-coupling, and optionally reaction with an acid. Compds. prepared by the processes of the invention have demonstrated activity as histamine-3 receptor ligands (no data).

IT 69498-23-3P 675624-33-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

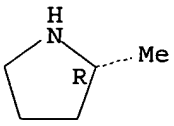
RN 69498-23-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

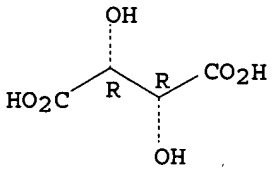
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

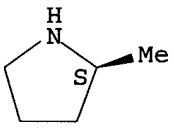


RN 675624-33-6 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

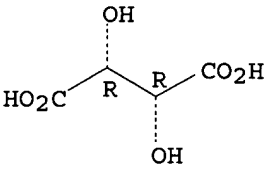
Absolute stereochemistry. Rotation (+).



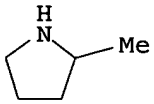
CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

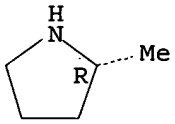


IT 765-38-8, 2-Methylpyrrolidine 117607-13-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)
RN 765-38-8 HCAPLUS
CN Pyrrolidine, 2-methyl- (CA INDEX NAME)



RN 117607-13-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrobromide (1:1), (2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

L5 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220081 HCAPLUS
DOCUMENT NUMBER: 140:253438
TITLE: Process for preparing amine-substituted benzofurans, in particular 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile, via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands
INVENTOR(S): Cowart, Marlon D.; Pu, Yu-Ming; Ku, Yi-Yin; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.; Faghih, Ramin; Gfesser, Gregory A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Division of U.S. Ser. No. 244,234, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004054185	A1	20040318	US 2003-613621		20030702
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	B3	20020916
			US 2002-411210P	P	20020916
			US 2003-654897	A3	20030905

OTHER SOURCE(S): CASREACT 140:253438; MARPAT 140:253438
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to processes for preparing amine substituted benzofurans I and salts, and more particularly 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile II, and salts as histamine-3 receptor ligands (no data) via halogenation, cyclization, (sulfonation), alkylation, and cross-coupling, and optionally reaction with an acid. The advantages include reduction or elimination of isolation and purification steps and high reaction yields, making the process efficient in preparation of high-grade pharmaceuticals. Specifically, I were prepared either by halogenation of phenol RAC6H4OH with a halogenating agent and an oxidant, cyclization with 3-butyn-1-ol of the o-halophenol (III) (halo = Br, I), sulfonation of the alc. with p-toluene/methane/trifluoromethane/sulfonic acid, alkylation of an (un)substituted pyrrolidine or piperidine to give the bromobenzofuran intermediate IV, and cross-coupling of IV with (un)substituted (HO)2B-R1 or by cyclization of III with an alkyne A(CH2)2CH.tplbond.C to give IV, followed by the above cross coupling [wherein A = (un)substituted pyrrolidinyl, piperidinyl; R1 = (un)substituted 4-cyanophenyl, hetero/aryl, RA = Br, Cl, (un)substituted 4-cyanophenyl, hetero/aryl]. For example, II•(L)-tartrate was prepared, in five steps, by iodination of 4'-hydroxy-1,1'-biphenyl-4-carbonitrile with N-iodosuccinimide in the presence of AcOH/H2SO4, cyclization in the presence of Pd(OAc)2/PPh3/Cu2I, tosylation of the hydroxybenzofuran, amination of the tosylate with (2R)-2-methylpyrrolidine tartrate, followed by salt formation with (L)-tartaric acid.

IT 670425-15-7 670425-20-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

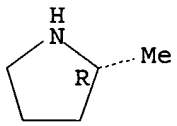
RN 670425-15-7 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

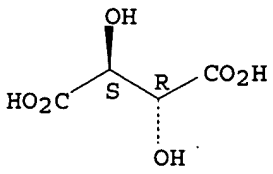
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.

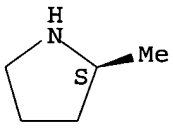


RN 670425-20-4 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

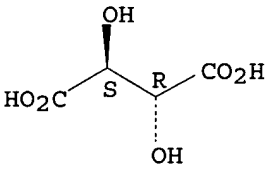
Absolute stereochemistry. Rotation (+).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.

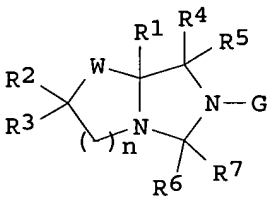


L5 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:931118 HCAPLUS
DOCUMENT NUMBER: 140:5047
TITLE: Preparation of pyrrolo[1,2-c]imidazoles as bicyclic modulators of androgen receptor function
INVENTOR(S): Sun, Chongqing; Hamann, Lawrence; Augeri, David; Bi, Yingzhi; Robl, Jeffrey; Huang, Yan-ting; Wang, Tammy; Simpkins, Ligaya; Holubec, Alexandra
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

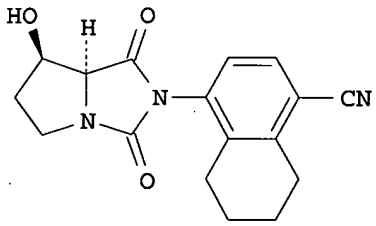
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003096980	A2	20031127	WO 2003-US15375		20030515
WO 2003096980	A3	20041021			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003234609	A1	20031202	AU 2003-234609		20030515
EP 1506178	A2	20050216	EP 2003-728951		20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005531555	T	20051020	JP 2004-504979		20030515
NO 2004004809	A	20050214	NO 2004-4809		20041104
PRIORITY APPLN. INFO.:			US 2002-381616P	P	20020517
			US 2002-406711P	P	20020829
			WO 2003-US15375	W	20030515

OTHER SOURCE(S): MARPAT 140:5047

GI



I



II

AB Title compds. I [R1 = H, (un)substituted-alkyl, -alkenyl, arylalkyl, etc.; R2 and R3 independently = H, halo, (un)substituted alkyl, -alkoxy, etc.; R4 and R5 independently = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, -arylalkyl, etc., wherein at least one of R4 and R5 is H, or R4 and R5 taken together can form a double bond with O, S, substituted N or C; R6 and R7 independently = H, (un)substituted-alkyl, -alkenyl, -heteroaryl, -aryl, etc., wherein at least one of R6 and R7 is H, or R6 and R7 taken together can form a double bond with O, S, substituted N or C; G = aryl, heterocyclo or heteroaryl group, wherein said group is mono- or polycyclic and optionally substituted; W = CR6R7, CR6OR8, CR6NR9R10; R8 = H, F2HC, F3C, COR9, (un)substituted alkyl; R9 and R10 independently = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, etc.; n = 1 or 2] and their pharmaceutically acceptable salts are prepared and disclosed as modulators of androgen receptor functions. Thus, e.g., II was prepared via acetylation of 5,6,7,8-tetrahydronaphthylamine, bromination, cyanation and reduction/oxidation sequence to provide 4-isocyanato-5,6,7,8-tetrahydronaphthalene-1-carbonitrile which was reacted with (2S,3R)-3-hydroxy-2-pyrrolidinecarboxylic acid Me ester trifluoroacetic acid salt. Numerous assays are described for evaluation of I (no data). Also provided are pharmaceutical compns. containing such compds. and

processes for preparing some of the compds. of the invention.

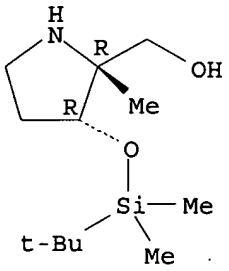
IT 627531-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolo[1,2-c]imidazoles as bicyclic modulators of androgen receptor function)

RN 627531-74-2 HCAPLUS
CN 2-Pyrrolidinemethanol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-, (2R,3R)-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

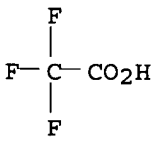
CRN 627531-73-1
CMF C12 H27 N O2 Si

Absolute stereochemistry.



CM 2

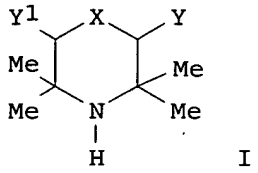
CRN 76-05-1
CMF C2 H F3 O2



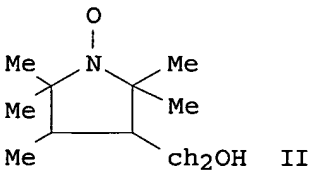
L5 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:690638 HCAPLUS
DOCUMENT NUMBER: 133:222194
TITLE: Process for preparing stereo hindered amine nitrogen-oxygen free radical
INVENTOR(S): Tian, He; Chen, Kongchang; Guo, Lin
PATENT ASSIGNEE(S): Huadong Univ. of Science and Engineering, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1235946	A	19991124	CN 1999-113523	19990312
CN 1086686	B	20020626		
PRIORITY APPLN. INFO.:			CN 1999-113523	19990312
OTHER SOURCE(S):	MARPAT 133:222194			

GI



I



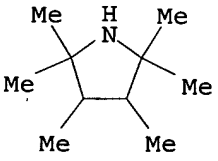
II

AB The process comprises oxidizing hindered amine with H2O2 in the presence of metal ion-loaded cation exchange resin in solvent at 20-100° for 3-16 h, recovering catalyst, and collecting product. The mole ratio of H2O2 to hindered amine is 1-4, and the ratio of catalyst to hindered amine is 1-10%. Title hindered amines are [I; X = CHOH, CH2, CHOCH3, C:O, HCOOCCH3, CHCl, CHOSO3H, CHBr, O, electron pair; Y = H, CH3, CHO, CH2OH, CONH2; Y1 = H, CH3]. The metal ions were Ca, Mg, Ba, Sr, Zn, and Sn2+. The cation exchange resin is styrene, acrylic, methacrylic, or phenolic cation exchange resin, and the ratio of cation ion to cation exchange resin is 2.0-10.0 mmol/g of dried resin. Thus, the title compound II was prepared

IT 2978-54-3, 2,2,3,4,5,5-Hexamethylpyrrolidine 77211-20-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing stereo hindered amine nitrogen-oxygen free radical)

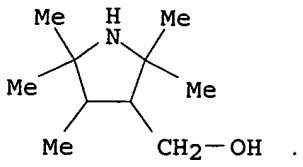
RN 2978-54-3 HCAPLUS

CN Pyrrolidine, 2,2,3,4,5,5-hexamethyl- (9CI) (CA INDEX NAME)



RN 77211-20-2 HCAPLUS

CN 3-Pyrrolidinemethanol, 2,2,4,5,5-pentamethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:41733 HCAPLUS
DOCUMENT NUMBER: 128:104026
TITLE: Process for preparing medium pore size zeolites using neutral amines
INVENTOR(S): Nakagawa, Yumi; Zones, Stacey I.
PATENT ASSIGNEE(S): Chevron U.S.A. Inc., USA
SOURCE: U.S., 8 pp., Cont.-in-part of U.S. Ser. No. 406,087, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5707600	A	19980113	US 1996-610449	19960304
WO 9629285	A1	19960926	WO 1996-US3283	19960308
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9651887	A	19961008	AU 1996-51887	19960308
EP 815053	A1	19980107	EP 1996-908747	19960308
EP 815053	B1	20030212		
R: CH, DE, FR, GB, IT, LI, NL, SE				
CN 1181744	A	19980513	CN 1996-193321	19960308
CN 1079371	B	20020220		
JP 11502187	T	19990223	JP 1996-528457	19960308
RU 2148554	C1	20000510	RU 1997-117371	19960308
EP 1110912	A2	20010627	EP 2001-100071	19960308
R: CH, DE, FR, GB, IT, LI, NL, SE				

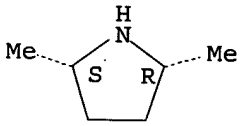
PRIORITY APPLN. INFO.:		
US 1995-406087	B2	19950317
US 1996-610449	A	19960304
EP 1996-908747	A3	19960308
WO 1996-US3283	W	19960308

AB The present invention relates to a process for preparing medium pore size zeolites using small, neutral amines capable of forming the zeolite, the amine containing (a) only carbon, nitrogen and hydrogen atoms, (b) one primary, secondary or tertiary, but not quaternary, amino group, and (c) a tertiary nitrogen atom, at least one tertiary carbon atom, or a nitrogen atom bonded directly to at least one secondary carbon atom, wherein the process is conducted in the absence of a quaternary ammonium compound

IT 39713-71-8, cis-2,5-Dimethylpyrrolidine
RL: TEM (Technical or engineered material use); USES (Uses)

(directing agent; process for preparing medium pore size zeolites using neutral amines)
RN 39713-71-8 HCAPLUS
CN Pyrrolidine, 2,5-dimethyl-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

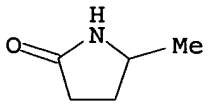
L5 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:293839 HCAPLUS
DOCUMENT NUMBER: 126:263854
TITLE: Process for preparing amido-carboxylic acid esters having internal amide linkages
INVENTOR(S): Lutz, Gary Paul; Zima, George Chester; Williams, Thomas Hugh
PATENT ASSIGNEE(S): Eastman Chemical Company, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9709299	A1	19970313	WO 1996-US14027		19960904
W: AU, CN, JP					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5717118	A	19980210	US 1995-523419		19950905
AU 9668643	A	19970327	AU 1996-68643		19960904
EP 874803	A1	19981104	EP 1996-929114		19960904
EP 874803	B1	20001227			
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE					
CN 1200724	A	19981202	CN 1996-197820		19960904
JP 11512389	T	19991026	JP 1996-511302		19960904
ES 2153123	T3	20010216	ES 1996-929114		19960904
PRIORITY APPLN. INFO.:			US 1995-523419	A	19950905
			WO 1996-US14027	W	19960904

OTHER SOURCE(S): MARPAT 126:263854
AB The present invention relates to a one-step process for preparing amido-carboxylic acid esters having the amide nitrogen positioned between two carbonyl carbons by reacting a carboxylic acid or carboxylic acid ester with a monohydric alc. and either a lactam, amino-carboxylic acid or a polymeric amino-carboxylic acid. In this process, amidation, esterification, alcoholysis, and hydrolysis reactions occur simultaneously.
IT 108-27-0, γ-Valerolactam
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amido-carboxylic acid esters having internal amide linkages)
RN 108-27-0 HCAPLUS

10789106.trn

CN 2-Pyrrolidinone, 5-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

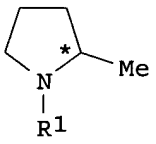


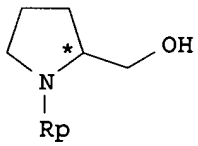
=> d l6 ibib abs hitstr tot

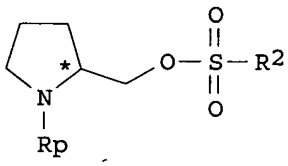
L6 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127154 HCAPLUS
DOCUMENT NUMBER: 142:74442
TITLE: Process for preparing 2-methylpyrrolidine and specific enantiomers thereof
INVENTOR(S): Ku, Yi-Yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

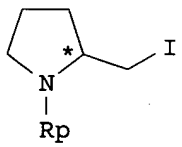
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004260100	A1	20041223	US 2004-789106		20040227
PRIORITY APPLN. INFO.:			US 2003-450480P	P	20030227

OTHER SOURCE(S): MARPAT 142:74442
GI


I


II


III


IV

AB The invention relates to a process for preparing 2-methylpyrrolidine or N-protected 2-methylpyrrolidine (I) (R1 = H, a nitrogen-protecting group; * denotes an asym. carbon atom) and, more particularly, specific enantiomers of I. The compound I is useful as an intermediate to obtain a compound useful for modulating a histamine-3 receptor. Novel intermediates also such as N-protected prolinol (II) (Rp = a nitrogen-protecting group) and their sulfonate ester (III) [Rp = same as above; R2 = each (un)substituted alkyl or aryl], and

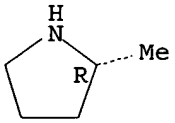
2-iodomethylpyrrolidine (IV) (Rp = same as above) are described. Thus, N-protection of (S)-prolinol by di-tert-Bu dicarbonate followed by esterification with methanesulfonyl chloride gave (S)-2-[(methanesulfonyloxy)methyl]pyrrolidine-1-carboxylic acid tert-Bu ester which was iodinated by NaI to give (S)-2-iodomethylpyrrolidine-1-carboxylic acid tert-Bu ester (V). Hydrogenolysis of V over 10% Pd-C gave (R)-2-methylpyrrolidine-1-carboxylic acid tert-Bu ester which was treated with HCl in EtOAc to give (R)-2-methylpyrrolidine hydrochloride.

IT 135324-85-5P, (R)-2-Methylpyrrolidine monohydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine, specific enantiomers thereof, and their intermediates from prolinol)

RN 135324-85-5 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L6 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:722955 HCAPLUS
DOCUMENT NUMBER: 141:243334
TITLE: An efficient and cost-effective process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol
INVENTOR(S): Ku, Yi-yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171845	A1	20040902	US 2003-376534	20030227
CA 2515801	A1	20040910	CA 2004-2515801	20040225
WO 2004076388	A2	20040910	WO 2004-US5573	20040225
WO 2004076388	A3	20041202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1601650	A2	20051207	EP 2004-714598	20040225

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006519233 T 20060824 JP 2006-503863 20040225
PRIORITY APPLN. INFO.: US 2003-376534 A 20030227
WO 2004-US5573 W 20040225

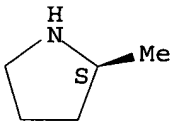
OTHER SOURCE(S): MARPAT 141:243334

AB The invention relates to an efficient and cost-effective process for preparing 2-methylpyrrolidine and, more particularly, specific enantiomers of 2-methylpyrrolidine, from (R/S)-prolinol. Novel intermediates also are described. The title compds. were synthesized in several steps via N-protection of corresponding chiral prolinols, conversion of the hydroxy groups to sulfonates or iodides, reduction and finally N-deprotection. The iodides could also be prepared from the corresponding sulfonates via reaction with metal iodides . Thus, (S)-prolinol was N-protected with tert-butoxycarbonyl anhydride (100% yield) followed by sulfonylation with mesyl chloride (96% yield). The resulting mesylate was either directly reduced to (R)-N-Boc-2-methylpyrrolidine with lithium triethoxyborohydride (54% yield) or via the iodide intermediate through iodination with LiI (79% yield) followed by hydrogenolysis in the presence of Pd/C (85.9% yield). (R)-N-Boc-2-methylpyrrolidine was then deprotected with HCl to give 2-(R)-methylpyrrolidine hydrochloride. (96% yield).

IT 59335-84-1P, 2-(S)-Methylpyrrolidine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

RN 59335-84-1 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)- (9CI) (CA INDEX NAME)

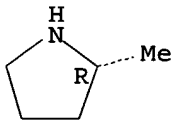
Absolute stereochemistry. Rotation (+).



IT 41720-98-3P, 2-(R)-Methylpyrrolidine 135324-85-5P, (R)-2-Methylpyrrolidine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target product; process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

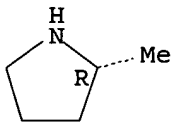
RN 41720-98-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 135324-85-5 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

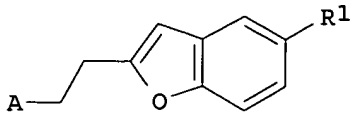


● HCl

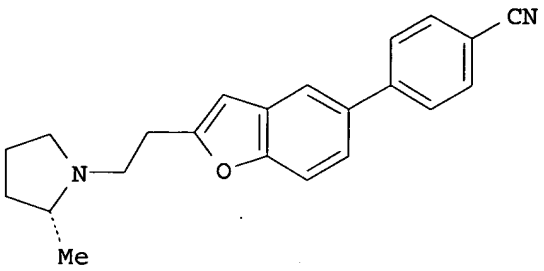
L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:252496 HCAPLUS
DOCUMENT NUMBER: 140:287256
TITLE: Process for preparing amine-substituted benzofurans
INVENTOR(S): Ku, Yi-yin; Pu, Yu-ming; Cowart, Marlon D.; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004024707	A2	20040325	WO 2003-US28396		20030910
WO 2004024707	A3	20040812			
W: CA, JP, MX					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
US 2004133007	A1	20040708	US 2003-654897		20030905
US 6822101	B2	20041123			
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	A	20020916
			US 2003-654897	A	20030905
			US 2002-411210P	P	20020916

OTHER SOURCE(S): CASREACT 140:287256; MARPAT 140:287256
GI



I



II

AB The present invention relates to processes for preparing amine substituted benzofurans, e.g. I [A = (substituted)pyrrolidinyl or (substituted)piperidinyl; R1 = (substituted)4-cyanophenyl, (substituted)aryl, (substituted)heteroaryl], and more particularly 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-1-benzofuran-5-yl)benzonitrile (II), were prepared via halogenation, cyclization, sulfonation, alkylation, and cross-coupling, and optionally reaction with an acid. Compds. prepared by the processes of the invention have demonstrated activity as histamine-3 receptor ligands (no data).

IT 69498-23-3P 675624-33-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

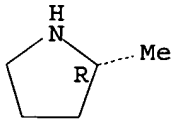
RN 69498-23-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

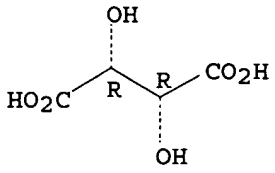
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

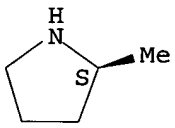


RN 675624-33-6 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

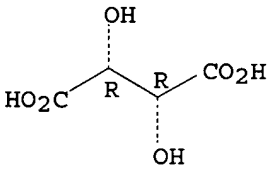
Absolute stereochemistry. Rotation (+).



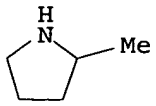
CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

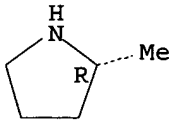


IT 765-38-8, 2-Methylpyrrolidine 117607-13-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)
RN 765-38-8 HCAPLUS
CN Pyrrolidine, 2-methyl- (CA INDEX NAME)



RN 117607-13-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrobromide (1:1), (2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220081 HCAPLUS
DOCUMENT NUMBER: 140:253438
TITLE: Process for preparing amine-substituted benzofurans, in particular 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile, via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands
INVENTOR(S): Cowart, Marlon D.; Pu, Yu-Ming; Ku, Yi-Yin; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.; Faghih, Ramin; Gfesser, Gregory A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Division of U.S. Ser. No. 244,234, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004054185	A1	20040318	US 2003-613621		20030702
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	B3	20020916
			US 2002-411210P	P	20020916
			US 2003-654897	A3	20030905

OTHER SOURCE(S): CASREACT 140:253438; MARPAT 140:253438
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to processes for preparing amine substituted benzofurans I and salts, and more particularly 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile II, and salts as histamine-3 receptor ligands (no data) via halogenation, cyclization, (sulfonation), alkylation, and cross-coupling, and optionally reaction with an acid. The advantages include reduction or elimination of isolation and purification steps and high reaction yields, making the process efficient in preparation of high-grade pharmaceuticals. Specifically, I were prepared either by halogenation of phenol RAC6H4OH with a halogenating agent and an oxidant, cyclization with 3-butyn-1-ol of the o-halophenol (III) (halo = Br, I), sulfonation of the alc. with p-toluene/methane/trifluoromethane/sulfonic acid, alkylation of an (un)substituted pyrrolidine or piperidine to give the bromobenzofuran intermediate IV, and cross-coupling of IV with (un)substituted (HO)2B-R1 or by cyclization of III with an alkyne A(CH2)2CH.tplbond.C to give IV, followed by the above cross coupling [wherein A = (un)substituted pyrrolidinyl, piperidinyl; R1 = (un)substituted 4-cyanophenyl, hetero/aryl, RA = Br, Cl, (un)substituted 4-cyanophenyl, hetero/aryl]. For example, II•(L)-tartrate was prepared, in five steps, by iodination of 4'-hydroxy-1,1'-biphenyl-4-carbonitrile with N-iodosuccinimide in the presence of AcOH/H2SO4, cyclization in the presence of Pd(OAc)2/PPh3/Cu2I, tosylation of the hydroxybenzofuran, amination of the tosylate with (2R)-2-methylpyrrolidine tartrate, followed by salt formation with (L)-tartaric acid.

IT 670425-15-7 670425-20-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

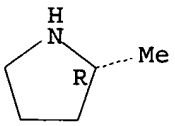
RN 670425-15-7 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

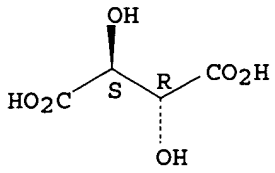
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.

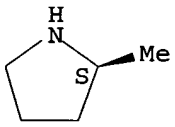


RN 670425-20-4 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

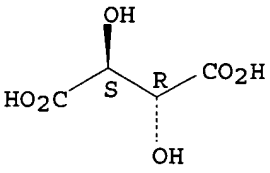
Absolute stereochemistry. Rotation (+).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.



=> d l8 ibib abs hitstr tot

L8 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:113504 HCAPLUS
TITLE: Preparation of spiro-cyclic compounds as acetyl-CoA carboxylase inhibitors
INVENTOR(S): Kamata, Makoto; Fukatsu, Kohji; Yamashita, Tohru; Furuyama, Naoki; Endo, Satoshi
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 450pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

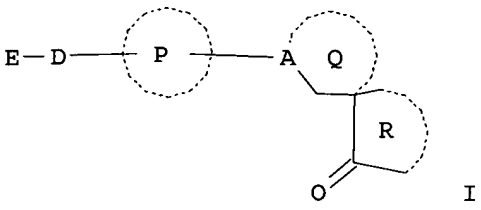
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007013691	A1	20070201	WO 2006-JP315447	20060728

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-221959 A 20050729
JP 2006-159117 A 20060607

GI



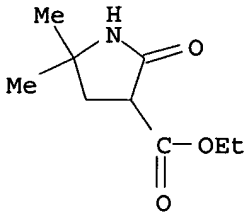
I

AB The title compds. I [E represents a cyclic group which may be substituted; D represents carbonyl or sulfonyl; A represents CH or N; the ring P represents a 5- to 7-membered ring which may be further substituted; the ring Q represents a 5- to 7-membered non-aromatic ring which may be further substituted; and the ring R represents a 5- to 7-membered non-aromatic ring which may be further substituted and which may be fused] are prepared I are useful for the prevention/treatment of obesity, diabetes, etc. Thus, 7-[1-(9-anthrylcarbonyl)piperidin-4-yl]-2-ethyl-2,7-diazaspiro[4.5]decan-1-one was prepared in a multistep process from piperidine-1,3-dicarboxylic acid 3-Et 1-tert-Bu ester and bromoacetonitrile. Several compds. of this invention showed IC50 values ≤ 10 nM against acetyl-CoA carboxylase 2. Formulations are given.

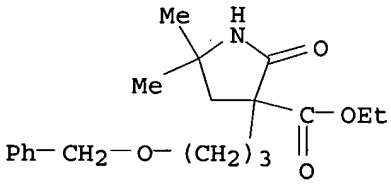
IT 923010-12-2P 923010-13-3P 923010-14-4P
923010-15-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of spiro-cyclic compds. as acetyl-CoA carboxylase inhibitors)

RN 923010-12-2 HCAPLUS

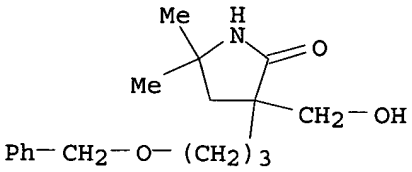
CN 3-Pyrrolidinecarboxylic acid, 5,5-dimethyl-2-oxo-, ethyl ester (CA INDEX NAME)



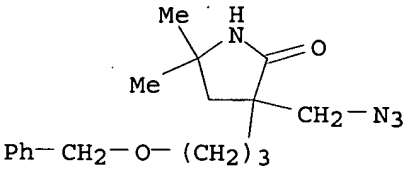
RN 923010-13-3 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 5,5-dimethyl-2-oxo-3-[3-(phenylmethoxy)propyl]-, ethyl ester (CA INDEX NAME)



RN 923010-14-4 HCAPLUS
CN 2-Pyrrolidinone, 3-(hydroxymethyl)-5,5-dimethyl-3-[3-(phenylmethoxy)propyl]- (CA INDEX NAME)



RN 923010-15-5 HCAPLUS
CN 2-Pyrrolidinone, 3-(azidomethyl)-5,5-dimethyl-3-[3-(phenylmethoxy)propyl]- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:680917 HCAPLUS
DOCUMENT NUMBER: 145:145750
TITLE: Preparation of pyrrolidine derivatives as dipeptidylpeptidase IV inhibitors
INVENTOR(S): Nakai, Hisao; Kondo, Takashi; Ota, Motohiro

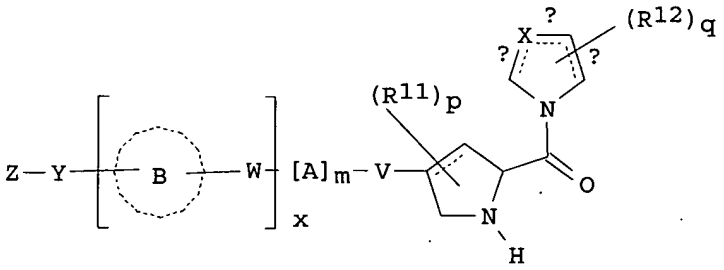
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006073167	A1	20060713	WO 2006-JP300061	20060106

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-3063 A 20050107
OTHER SOURCE(S): MARPAT 145:145750
GI



I

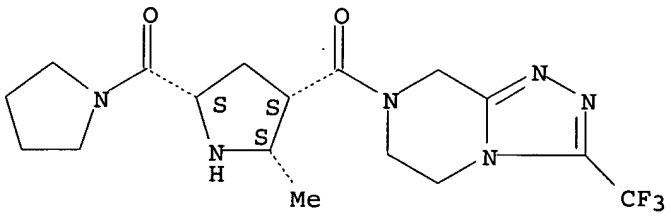
AB The title compds. I [V, W and Y represent each a bond or a spacer having from 1 to 8 atoms in the main chain; the rings A and B are each a cyclic group optionally further having substituent(s); Z represents H or a substituent; X represents carbon or sulfur; R11 and R12 represent each a substituent; p and q are each 0 or an integer of 1 to 4; and x and m are each 0 or 1; the dotted line indicates a single bond or a double bond; α and β or β and γ do not represent double bonds at the same time; when X is S, both α and β indicate single bonds] are prepared Thus, 1-(3-methyl-1,2,4-thiadiazol-5-yl)-4-([(3S,5S)-5-(pyrrolidin-1-ylcarbonyl)pyrrolidin-3-yl]carbonyl)piperazine hydrochloride was prepared in a multistep process from 2-benzyl 1-tert-Bu (2S,4S)-4-cyano-1,2-pyrrolidinedicarboxylate. Compds. of this invention showed IC50 values of 18 nM to 52 nM against dipeptidylpeptidase IV. Formulations are given.

IT 862079-17-2P 898273-51-3P 898275-08-6P
898275-14-4P 898275-16-6P 898275-18-8P
898275-20-2P 898275-22-4P 898275-23-5P
898275-24-6P 898275-25-7P 898275-26-8P
898275-27-9P 898275-28-0P 898275-29-1P

898275-30-4P 898275-31-5P 898275-92-8P
898276-01-2P 898276-03-4P 898276-06-7P
898276-08-9P 898276-09-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine derivs. as dipeptidylpeptidase IV inhibitors)

RN 862079-17-2 HCAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 5,6,7,8-tetrahydro-7-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

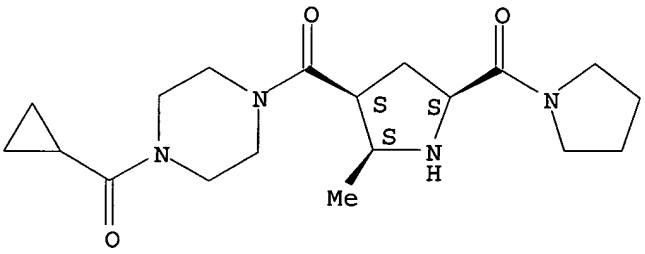
Absolute stereochemistry.



● HCl

RN 898273-51-3 HCAPLUS
CN Piperazine, 1-(cyclopropylcarbonyl)-4-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

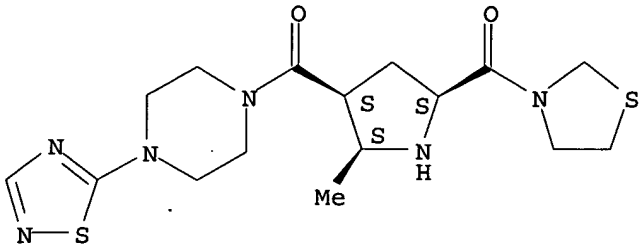
Absolute stereochemistry.



● HCl

RN 898275-08-6 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(1,2,4-thiadiazol-5-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

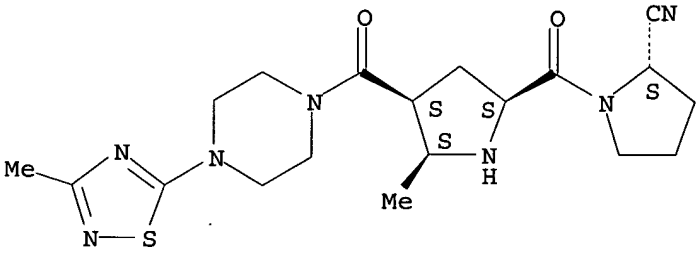


RN 898275-14-4 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-5-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-2-methyl-3-pyrrolidinyl]carbonyl]-4-(3-methyl-1,2,4-thiadiazol-5-yl)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

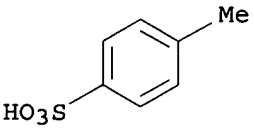
CRN 898275-13-3
CMF C19 H27 N7 O2 S

Absolute stereochemistry.



CM 2

CRN 104-15-4
CMF C7 H8 O3 S

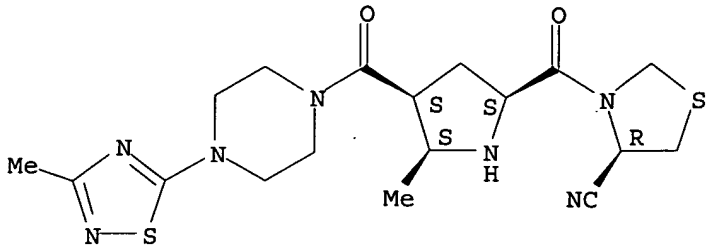


RN 898275-16-6 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-5-[[(4R)-4-cyano-3-thiazolidinyl]carbonyl]-2-methyl-3-pyrrolidinyl]carbonyl]-4-(3-methyl-1,2,4-thiadiazol-5-yl)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

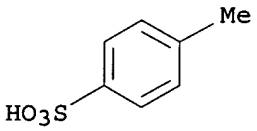
CRN 898275-15-5
CMF C18 H25 N7 O2 S2

Absolute stereochemistry.



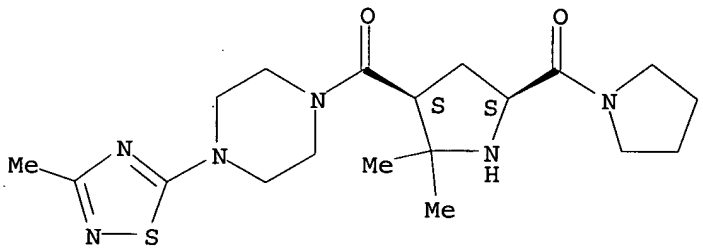
CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RN 898275-18-8 HCAPLUS
CN Piperazine, 1-[[(3S,5S)-2,2-dimethyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(3-methyl-1,2,4-thiadiazol-5-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

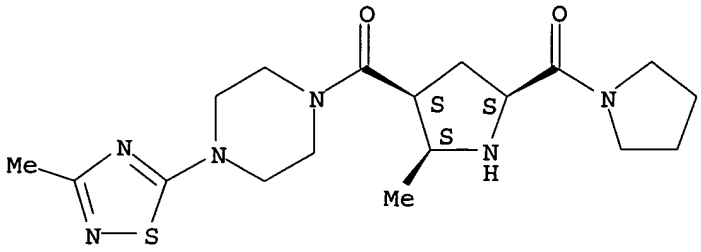
Absolute stereochemistry.



● HCl

RN 898275-20-2 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(3-methyl-1,2,4-thiadiazol-5-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



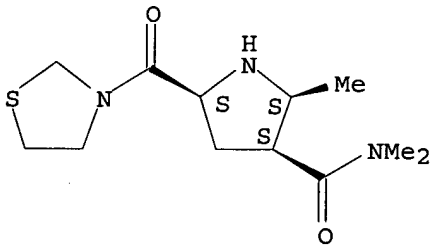
● HCl

RN 898275-22-4 HCAPLUS
CN 3-Pyrrolidinecarboxamide, N,N,2-trimethyl-5-(3-thiazolidinylcarbonyl)-, (2S,3S,5S)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

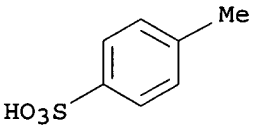
CRN 898275-21-3
CMF C12 H21 N3 O2 S

Absolute stereochemistry.



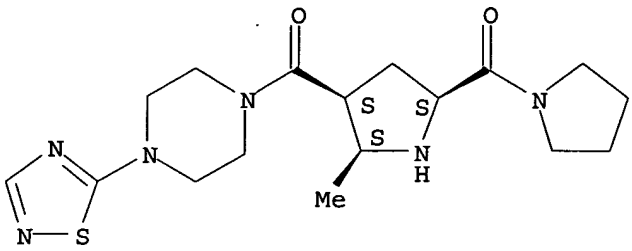
CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RN 898275-23-5 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(1,2,4-thiadiazol-5-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

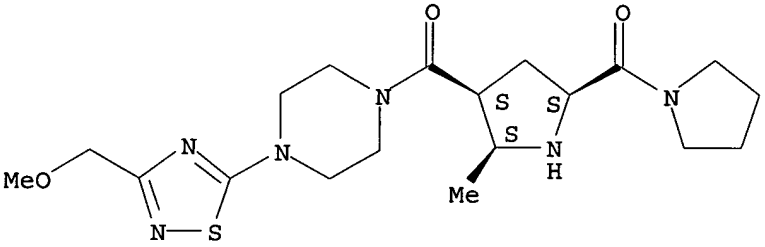
Absolute stereochemistry.



● HCl

RN 898275-24-6 HCAPLUS
CN Piperazine, 1-[3-(methoxymethyl)-1,2,4-thiadiazol-5-yl]-4-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

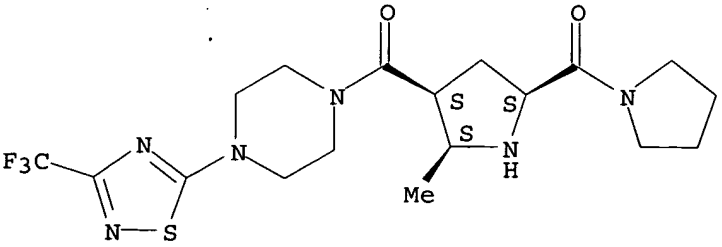
Absolute stereochemistry.



● HCl

RN 898275-25-7 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-[3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

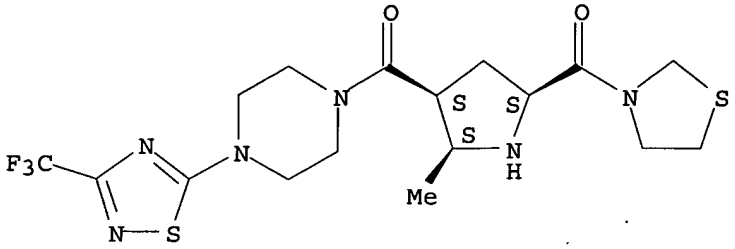
Absolute stereochemistry.



● HCl

RN 898275-26-8 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-[3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

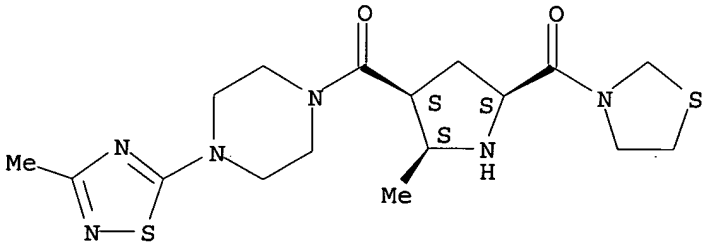
Absolute stereochemistry.



● HCl

RN 898275-27-9 HCAPLUS
CN Piperazine, 1-(3-methyl-1,2,4-thiadiazol-5-yl)-4-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

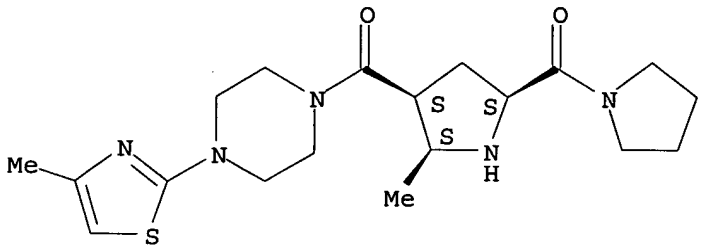
Absolute stereochemistry.



● HCl

RN 898275-28-0 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(4-methyl-2-thiazolyl)-, monohydrochloride (9CI) (CA INDEX NAME)

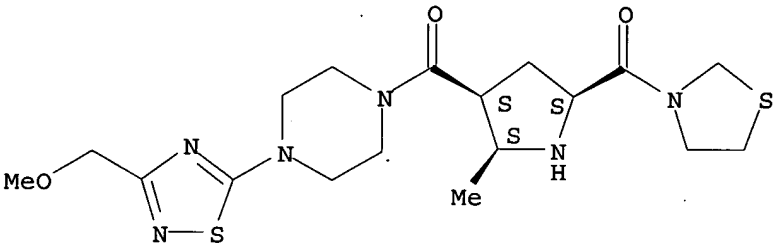
Absolute stereochemistry.



● HCl

RN 898275-29-1 HCAPLUS
CN Piperazine, 1-[3-(methoxymethyl)-1,2,4-thiadiazol-5-yl]-4-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

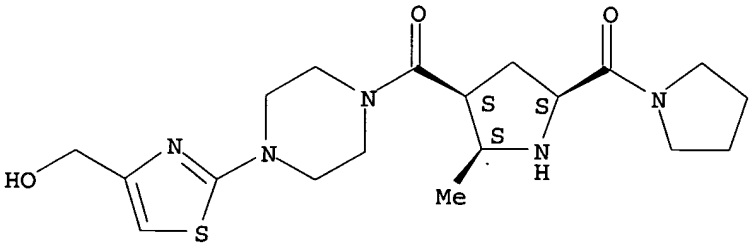
Absolute stereochemistry.



● HCl

RN 898275-30-4 HCAPLUS
CN Piperazine, 1-[4-(hydroxymethyl)-2-thiazolyl]-4-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

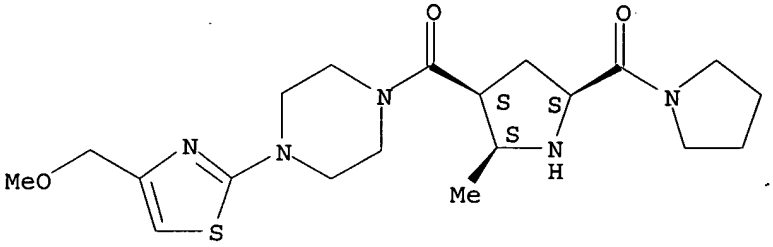
Absolute stereochemistry.



● HCl

RN 898275-31-5 HCAPLUS
CN Piperazine, 1-[4-(methoxymethyl)-2-thiazolyl]-4-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

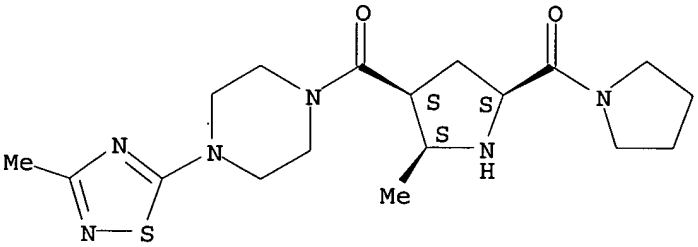
Absolute stereochemistry.



● HCl

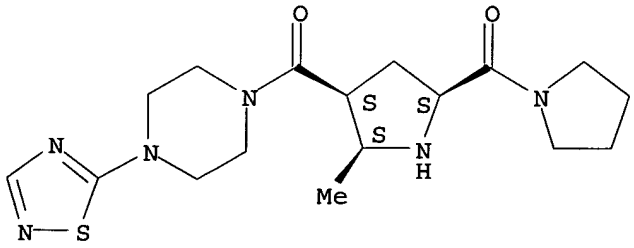
RN 898275-92-8 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(3-methyl-1,2,4-thiadiazol-5-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 898276-01-2 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-(1,2,4-thiadiazol-5-yl)- (9CI) (CA INDEX NAME)

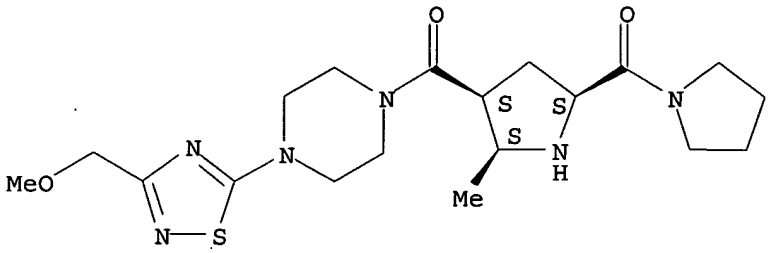
Absolute stereochemistry.



RN 898276-03-4 HCAPLUS
CN Piperazine, 1-[3-(methoxymethyl)-1,2,4-thiadiazol-5-yl]-4-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]- (9CI) (CA

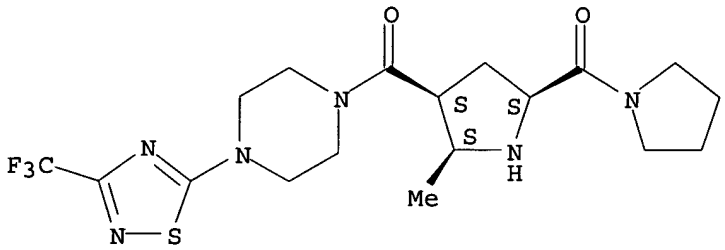
INDEX NAME)

Absolute stereochemistry.



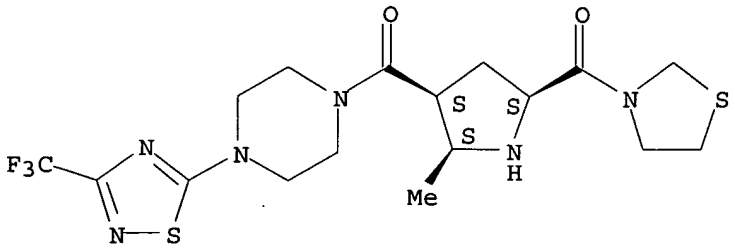
RN 898276-06-7 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(1-pyrrolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-[3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



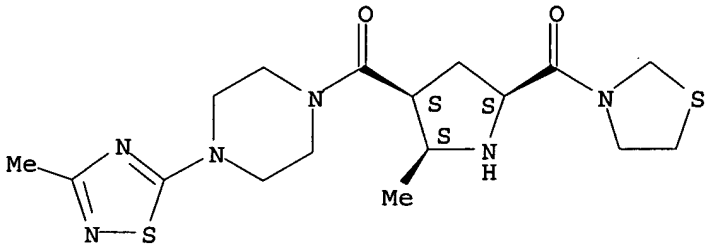
RN 898276-08-9 HCAPLUS
CN Piperazine, 1-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]-4-[3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



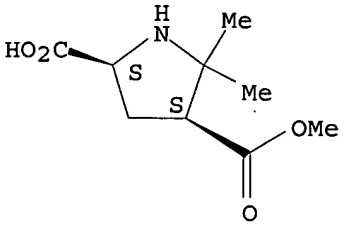
RN 898276-09-0 HCAPLUS
CN Piperazine, 1-(3-methyl-1,2,4-thiadiazol-5-yl)-4-[[(2S,3S,5S)-2-methyl-5-(3-thiazolidinylcarbonyl)-3-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



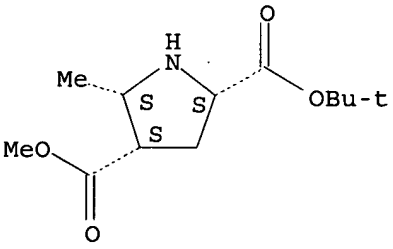
IT 404891-60-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrrolidine derivs. as dipeptidylpeptidase IV inhibitors)
RN 404891-60-7 HCAPLUS
CN 2,4-Pyrrolidinedicarboxylic acid, 5,5-dimethyl-, 4-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 862079-69-4P 862079-71-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidine derivs. as dipeptidylpeptidase IV inhibitors)
RN 862079-69-4 HCAPLUS
CN 2,4-Pyrrolidinedicarboxylic acid, 5-methyl-, 2-(1,1-dimethylethyl) 4-methyl ester, (2S,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

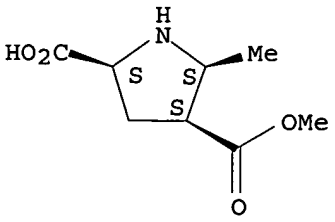


RN 862079-71-8 HCAPLUS
CN 2,4-Pyrrolidinedicarboxylic acid, 5-methyl-, 4-methyl ester, (2S,4S,5S)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

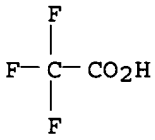
CRN 862079-70-7
CMF C8 H13 N O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:238601 HCAPLUS
DOCUMENT NUMBER: 144:311923
TITLE: Preparation of carbamoyl-substituted spiro compounds as histamine H3 antagonists or inverse agonists
INVENTOR(S): Jitsuoka, Makoto; Sato, Nagaaki; Tsukahara, Daisuke; Ohtake, Norikazu; Tokita, Shigeru
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 230 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

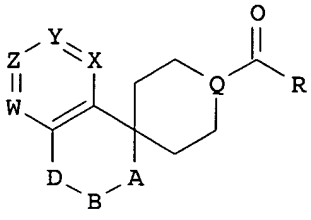
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006028239	A1	20060316	WO 2005-JP16692	20050906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-259258 A 20040907
JP 2004-344270 A 20041129

OTHER SOURCE(S): MARPAT 144:311923

GI



I

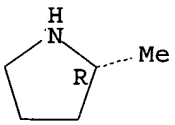
AB The title compds. I [X, Y, Z, W = (un)substituted methine; A = CO, O, NR5, etc.; B = NR50, O, CO, etc.; D = O, NR51, CO, etc.; Q = methine, N; R5 = H, alkyl, aryl, etc.; R50, R51 = H, alkyl; R = (un)substituted N(R6)CH2CH2NR7R8, etc.; R6 = H, alkyl; R7, R8 = alkyl, cycloalkyl, aralkyl, etc.; further details on R7 and R8 are given] are prepared They are useful in the prevention or treatment of metabolic diseases, circulatory diseases, etc. Thus, trans-5'-(2-fluoroethoxy)-3'-oxo-N-methyl-N-(2-piperidin-1-ylethyl)-spiro[cyclohexane-1,1'-(3'H)-isobenzofuran]-4-carboxamide HCl salt was prepared in a multistep process starting from Me 3-hydroxybenzoate. Compds. of this invention showed IC50 values of 0.08 nM to 9 nM in an assay for histamine H3 receptor binding inhibition.

IT 117607-13-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of carbamoyl-substituted spiro compds. as histamine H3 antagonists or inverse agonists)

RN 117607-13-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrobromide (1:1), (2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:79402 HCAPLUS

DOCUMENT NUMBER: 144:171020

TITLE: Preparation of aminothiazole moiety-containing heterocyclic compounds as selective inhibitors of Cdk4 and Cdk6

INVENTOR(S): Iwasawa, Yoshikazu; Shibata, Jun; Shimamura, Tadashi; Kurihara, Hideki; Mita, Takashi; Kawanishi, Nobuhiko;

Hashihayata, Takashi; Kawamura, Mikako; Sagara, Takeshi; Arai, Sachie; Hirai, Hiroshi
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 178 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006008874	A1	20060126	WO 2005-JP9593	20050519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005264213	A1	20060126	AU 2005-264213	20050519
CA 2567569	A1	20060126	CA 2005-2567569	20050519
EP 1754706	A1	20070221	EP 2005-743671	20050519
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LV				

PRIORITY APPLN. INFO.: JP 2004-178974 A 20040521
WO 2005-JP9593 W 20050519

OTHER SOURCE(S): MARPAT 144:171020
GI

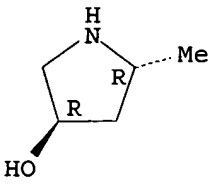
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [X is O, S, NH, or CH2; Y1, Y2, Y3, Y4 and Y5 are each independently CH or N with at least one of Y1 - Y5 being N; Z1 and Z2 are each independently CH or N; n is an integer of 1 to 3; R1 is C3-8 (un)substituted cycloalkyl, C6-10 (un)substituted aryl, an (un)substituted aliphatic or aromatic heterocycle, etc.; R2 and R3 are each independently hydrogen, lower (un)substituted alkyl, lower (un)substituted alkenyl, etc.; and R4 is hydrogen, lower alkyl, C3-6 cycloalkyl, etc.] are prepared Thus, the title compound II was prepared in a multistep process starting from 5-methyl-2-pyrazinecarboxylic acid. Compds. of this invention showed IC50 values of 3.9 nM to 20 nM against Cdk4 (cyclin dependent kinase 4).

IT 688810-07-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminothiazole moiety-containing heterocyclic compds. as selective inhibitors of Cdk4 and Cdk6)

RN 688810-07-3 HCAPLUS
CN 3-Pyrrolidinol, 5-methyl-, (3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

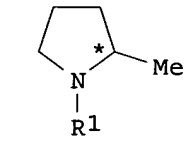


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

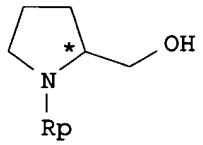
L8 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127154 HCAPLUS
DOCUMENT NUMBER: 142:74442
TITLE: Process for preparing 2-methylpyrrolidine and specific enantiomers thereof
INVENTOR(S): Ku, Yi-Yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004260100	A1	20041223	US 2004-789106		20040227
PRIORITY APPLN. INFO.:			US 2003-450480P	P	20030227

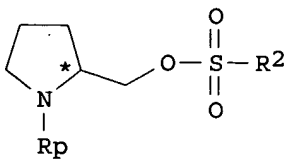
OTHER SOURCE(S): MARPAT 142:74442
GI



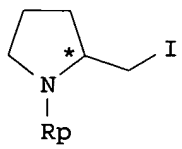
I



II



III



IV

AB The invention relates to a process for preparing 2-methylpyrrolidine or N-protected 2-methylpyrrolidine (I) (R1 = H, a nitrogen-protecting group; * denotes an asym. carbon atom) and, more particularly, specific enantiomers of I. The compound I is useful as an intermediate to obtain a compound useful for modulating a histamine-3 receptor. Novel intermediates also such as N-protected prolinol (II) (Rp = a nitrogen-protecting group) and their sulfonate ester (III) [Rp = same as above; R2 = each (un)substituted alkyl or aryl], and 2-iodomethylpyrrolidine (IV) (Rp = same as above) are described. Thus, N-protection of (S)-prolinol by di-tert-Bu dicarbonate followed by esterification with methanesulfonyl chloride gave (S)-2-

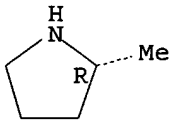
[(methanesulfonyloxy)methyl]pyrrolidine-1-carboxylic acid tert-Bu ester which was iodinated by NaI to give (S)-2-iodomethylpyrrolidine-1-carboxylic acid tert-Bu ester (V). Hydrogenolysis of V over 10% Pd-C gave (R)-2-methylpyrrolidine-1-carboxylic acid tert-Bu ester which was treated with HCl in EtOAc to give (R)-2-methylpyrrolidine hydrochloride.

IT 135324-85-5P, (R)-2-Methylpyrrolidine monohydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine, specific enantiomers thereof, and their intermediates from prolinol)

RN 135324-85-5 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L8 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:722955 HCAPLUS
DOCUMENT NUMBER: 141:243334
TITLE: An efficient and cost-effective process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol
INVENTOR(S): Ku, Yi-yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171845	A1	20040902	US 2003-376534	20030227
CA 2515801	A1	20040910	CA 2004-2515801	20040225
WO 2004076388	A2	20040910	WO 2004-US5573	20040225
WO 2004076388	A3	20041202		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1601650	A2	20051207	EP 2004-714598	20040225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006519233	T	20060824	JP 2006-503863	20040225

PRIORITY APPLN. INFO.: US 2003-376534 A 20030227

WO 2004-US5573 W 20040225

OTHER SOURCE(S): MARPAT 141:243334

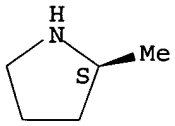
AB The invention relates to an efficient and cost-effective process for preparing 2-methylpyrrolidine and, more particularly, specific enantiomers of 2-methylpyrrolidine, from (R/S)-prolinol. Novel intermediates also are described. The title compds. were synthesized in several steps via N-protection of corresponding chiral prolinols, conversion of the hydroxy groups to sulfonates or iodides, reduction and finally N-deprotection. The iodides could also be prepared from the corresponding sulfonates via reaction with metal iodides . Thus, (S)-prolinol was N-protected with tert-butoxycarbonyl anhydride (100% yield) followed by sulfonylation with mesyl chloride (96% yield). The resulting mesylate was either directly reduced to (R)-N-Boc-2-methylpyrrolidine with lithium triethoxyborohydride (54% yield) or via the iodide intermediate through iodination with LiI (79% yield) followed by hydrogenolysis in the presence of Pd/C (85.9% yield). (R)-N-Boc-2-methylpyrrolidine was then deprotected with HCl to give 2-(R)-methylpyrrolidine hydrochloride (96% yield).

IT 59335-84-1P, 2-(S)-Methylpyrrolidine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

RN 59335-84-1 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

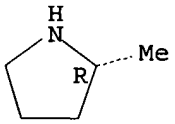


IT 41720-98-3P, 2-(R)-Methylpyrrolidine 135324-85-5P, (R)-2-Methylpyrrolidine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target product; process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

RN 41720-98-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)- (9CI) (CA INDEX NAME)

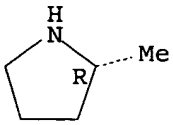
Absolute stereochemistry. Rotation (-).



RN 135324-85-5 HCAPLUS

CN Pyrrolidine, 2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

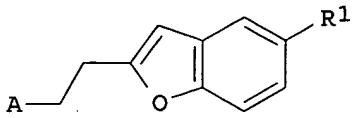


● HCl

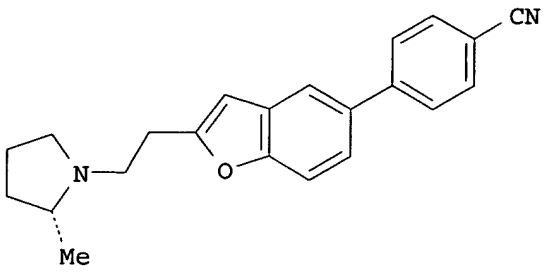
L8 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:252496 HCAPLUS
DOCUMENT NUMBER: 140:287256
TITLE: Process for preparing amine-substituted benzofurans
INVENTOR(S): Ku, Yi-yin; Pu, Yu-ming; Cowart, Marlon D.; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004024707	A2	20040325	WO 2003-US28396		20030910
WO 2004024707	A3	20040812			
W: CA, JP, MX					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
US 2004133007	A1	20040708	US 2003-654897		20030905
US 6822101	B2	20041123			
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	A	20020916
			US 2003-654897	A	20030905
			US 2002-411210P	P	20020916

OTHER SOURCE(S): CASREACT 140:287256; MARPAT 140:287256
GI



I .



II

AB The present invention relates to processes for preparing amine substituted benzofurans, e.g. I [A = (substituted)pyrrolidinyl or (substituted)piperidinyl; R1 = (substituted)4-cyanophenyl, (substituted)aryl, (substituted)heteroaryl], and more particularly 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-1-benzofuran-5-yl)benzonitrile (II), were prepared via halogenation, cyclization, sulfonation, alkylation, and cross-coupling, and optionally reaction with an acid. Compds. prepared by the processes of the invention have demonstrated activity as histamine-3 receptor ligands (no data).

IT 69498-23-3P 675624-33-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

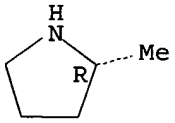
RN 69498-23-3 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

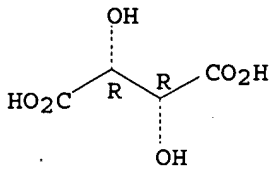
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

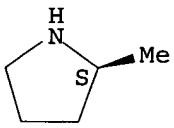


RN 675624-33-6 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

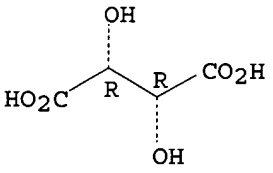
Absolute stereochemistry. Rotation (+).



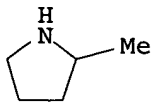
CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

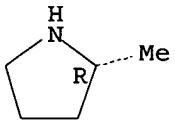


IT 765-38-8, 2-Methylpyrrolidine 117607-13-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)
RN 765-38-8 HCAPLUS
CN Pyrrolidine, 2-methyl- (CA INDEX NAME)



RN 117607-13-3 HCAPLUS
CN Pyrrolidine, 2-methyl-, hydrobromide (1:1), (2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

L8 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220081 HCAPLUS
DOCUMENT NUMBER: 140:253438
TITLE: Process for preparing amine-substituted benzofurans, in particular 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile, via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands
INVENTOR(S): Cowart, Marlon D.; Pu, Yu-Ming; Ku, Yi-Yin; Grieme, Timothy A.; Gupta, Ashok K.; Plata, Daniel J.; Faghih, Ramin; Gfesser, Gregory A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Division of U.S. Ser. No. 244,234, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004054185	A1	20040318	US 2003-613621		20030702
US 2005054677	A1	20050310	US 2004-946192		20040921
PRIORITY APPLN. INFO.:			US 2002-244234	B3	20020916
			US 2002-411210P	P	20020916
			US 2003-654897	A3	20030905

OTHER SOURCE(S): CASREACT 140:253438; MARPAT 140:253438
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to processes for preparing amine substituted benzofurans I and salts, and more particularly 4-[2-[2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl]-benzofuran-5-yl]benzonitrile II, and salts as histamine-3 receptor ligands (no data) via halogenation, cyclization, (sulfonation), alkylation, and cross-coupling, and optionally reaction with an acid. The advantages include reduction or elimination of isolation and purification steps and high reaction yields, making the process efficient in preparation of high-grade pharmaceuticals. Specifically, I were prepared either by halogenation of phenol RAC6H4OH with a halogenating agent and an oxidant, cyclization with 3-butyn-1-ol of the o-halophenol (III) (halo = Br, I), sulfonation of the alc. with p-toluene/methane/trifluoromethane/sulfonic acid, alkylation of an (un)substituted pyrrolidine or piperidine to give the bromobenzofuran intermediate IV, and cross-coupling of IV with (un)substituted (HO)2B-R1 or by cyclization of III with an alkyne A(CH2)2CH.tplbond.C to give IV, followed by the above cross coupling [wherein A = (un)substituted pyrrolidinyl, piperidinyl; R1 = (un)substituted 4-cyanophenyl, hetero/aryl, RA = Br, Cl, (un)substituted 4-cyanophenyl, hetero/aryl]. For example, II•(L)-tartrate was prepared, in five steps, by iodination of 4'-hydroxy-1,1'-biphenyl-4-carbonitrile with N-iodosuccinimide in the presence of AcOH/H2SO4, cyclization in the presence of Pd(OAc)2/PPh3/Cu2I, tosylation of the hydroxybenzofuran, amination of the tosylate with (2R)-2-methylpyrrolidine tartrate, followed by salt formation with (L)-tartaric acid.

IT 670425-15-7 670425-20-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; process for preparing amine-substituted benzofurans via halogenation, cyclization, sulfonation, amination, and cross-coupling, for use as histamine-3 receptor ligands)

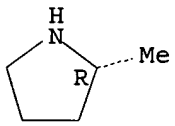
RN 670425-15-7 HCAPLUS

CN Pyrrolidine, 2-methyl-, (2R)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 41720-98-3
CMF C5 H11 N

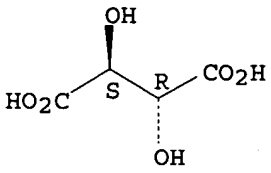
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.

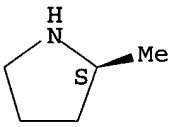


RN 670425-20-4 HCAPLUS
CN Pyrrolidine, 2-methyl-, (2S)-, rel-(2R,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59335-84-1
CMF C5 H11 N

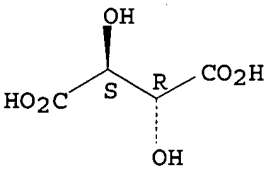
Absolute stereochemistry. Rotation (+).



CM 2

CRN 147-73-9
CMF C4 H6 O6

Relative stereochemistry.



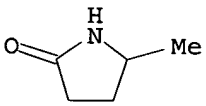
L8 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:333008 HCAPLUS
DOCUMENT NUMBER: 125:127644
TITLE: Method for obtaining improved image contrast in migration imaging members
INVENTOR(S): Limburg, William W.; Mammino, Joseph; Liebermann, George; Griffiths, Clifford H.; Shahin, Michael M.; Malhotra, Shadi L.; Chen, Liqin; Perron, Marie-Eve
PATENT ASSIGNEE(S): Xerox Corp., USA
SOURCE: U.S., 147 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514505	A	19960507	US 1995-441360	19950515
CA 2169980	A1	19961116	CA 1996-2169980	19960221
CA 2169980	C	20010424		
JP 08314240	A	19961129	JP 1996-113456	19960508
EP 743573	A2	19961120	EP 1996-303359	19960514
EP 743573	A3	19970305		
EP 743573	B1	20000906		
R: DE, FR, GB				

PRIORITY APPLN. INFO.: US 1995-441360 A 19950515
OTHER SOURCE(S): MARPAT 125:127644

AB Disclosed is a process which comprises (a) providing a migration imaging member comprising (1) a substrate and (2) a softenable layer comprising a softenable material and a photosensitive migration marking material present in the softenable layer as a monolayer of particles situated at or near the surface of the softenable layer spaced from the substrate, (b) uniformly charging the imaging member, (c) imagewise exposing the charged imaging member to activating radiation at a wavelength to which the migration marking material is sensitive, (d) causing the softenable material to soften and enabling a first portion of the migration marking material to migrate through the softenable material toward the substrate in an imagewise pattern while a second portion of the migration marking material remains substantially unmigrated within the softenable layer, and (e) contacting the second portion of the migration marking material with a transparentizing agent which transparentizes the migration marking material.

IT 108-27-0
RL: DEV (Device component use); TEM (Technical or engineered material use); USES (Uses)
(transparentizing agent for electrophotog. migration imaging members)
RN 108-27-0 HCAPLUS
CN 2-Pyrrolidinone, 5-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:76286 HCAPLUS
DOCUMENT NUMBER: 110:76286
TITLE: Process for polymerizing (alpha)-olefin
INVENTOR(S): Kioka, Mamoru; Kashiwa, Norio; Kimura, Tomohiko; Tomura, Mitsuo; Sotoyama, Toshiki
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8806163	A1	19880825	WO 1988-JP153	19880216
W: KR, US				

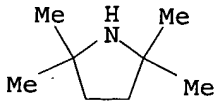
RW: AT, DE, FR, GB, IT, NL					
JP 63199702	A	19880818	JP 1987-32507		19870217
JP 08013857	B	19960214			
JP 63199703	A	19880818	JP 1987-32508		19870217
JP 08013858	B	19960214			
JP 63202603	A	19880822	JP 1987-34605		19870219
JP 63202604	A	19880822	JP 1987-34606		19870219
JP 07096567	B	19951018			
JP 09104714	A	19970422	JP 1996-244051		19870219
EP 303704	A1	19890222	EP 1988-901647		19880216
EP 303704	B1	19921223			
R: AT, DE, FR, GB, IT, NL					
AT 83783	T	19930115	AT 1988-901647		19880216
CN 1041764	A	19900502	CN 1988-107879		19881014
CA 1328100	C	19940329	CA 1988-581086		19881024
US 6121393	A	20000919	US 1995-418879		19950407
PRIORITY APPLN. INFO.:			JP 1987-32507	A	19870217
			JP 1987-32508	A	19870217
			JP 1987-34605	A	19870219
			JP 1987-34606	A	19870219
			EP 1988-901647	A	19880216
			WO 1988-JP153	A	19880216
			US 1988-280722	B1	19881012
			US 1991-715850	B1	19910617
			US 1993-90642	B1	19930713

AB Stereoregular polyolefins are prepared with highly active catalysts containing Ti chloride components, organometallic compds. or Group I-III metals, organic halogen compds. or transition metal compds., and organosilicon compds. or sterically hindered amines. The catalysts are prepared by contacting the components in the absence of α olefins or by conducting prepolymn. of α-olefins in the presence of the catalyst components optionally containing the final components. Thus, polypropylene having isotacticity index 97.9% was prepared at 14,600 g polymer/g catalyst in the presence of a solid Ti component containing Ti 2.4, Cl 56, Mg 19, and diiso-Bu phthalate 13.6% treated with Et3Al and Ph2Si(OMe)2 and tert-BuCl, Et3Al, and Ph2Si(OMe)2.

IT 4567-22-0
RL: CAT (Catalyst use); USES (Uses)
(catalyst components, for stereospecific polymerization of olefins)

RN 4567-22-0 HCAPLUS

CN Pyrrolidine, 2,2,5,5-tetramethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L8 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:195815 HCAPLUS

DOCUMENT NUMBER: 106:195815

TITLE: Palladium-catalyzed carbonylation of alkynes. II. Aspects of additive, oxidative, and reductive carbonylation

AUTHOR(S): Chiusoli, Gian Paolo; Costa, Mirco; Pergreffi, Paola; Reverberi, Sara; Salerno, Giuseppe

CORPORATE SOURCE: Ist. Chim. Org., Univ. Parma, Parma, I-43100, Italy

SOURCE: Gazzetta Chimica Italiana (1985), 115(12, Pt. B),

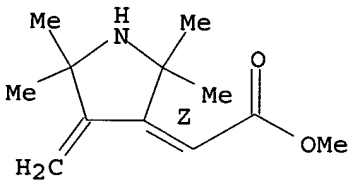
691-6
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:195815

AB The palladium-catalyzed carbonylation of alkynes using Pd halides complexes with thiourea as catalysts has led mainly to products deriving from additive carbonylation when substituents are present on the C atoms α to the triple bonds. While 1,6-dialkynes react readily, monoalkynes bearing alkyl groups on the carbon atom α to the triple bond react very sluggishly unless coordinating (acylamido) groups are present. With terminal alkynes, oxidative and reductive carbonylation occur simultaneously in the absence of oxygen, the hydrogen liberated by the former process being used for the latter. The steric effects observed with PdCl2-thiourea catalytic system result from contributions of both substrate substituents and thiourea. When PdI2 is used, in the absence of thiourea, oxidative carbonylation with a CO/O2 mixture becomes predominant even in the absence of substituents.

IT 88329-31-1P 88329-32-2P 108086-62-0P
108086-63-1P 108086-64-2P
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in palladium-catalyzed carbonylation of tetramethyldipropargylamine)

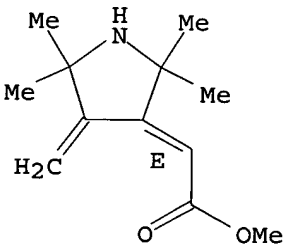
RN 88329-31-1 HCAPLUS
CN Acetic acid, (2,2,5,5-tetramethyl-4-methylene-3-pyrrolidinylidene)-, methyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



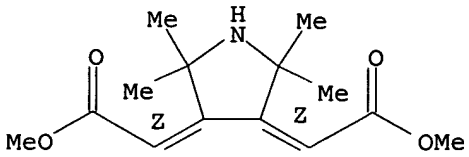
RN 88329-32-2 HCAPLUS
CN Acetic acid, (2,2,5,5-tetramethyl-4-methylene-3-pyrrolidinylidene)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



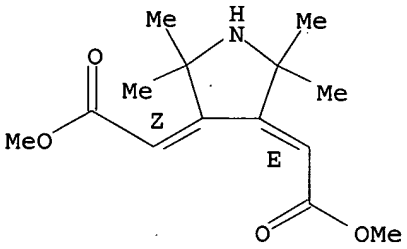
RN 108086-62-0 HCAPLUS
CN Acetic acid, 2,2'-(2,2,5,5-tetramethyl-3,4-pyrrolidinediylidene)bis-, dimethyl ester, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



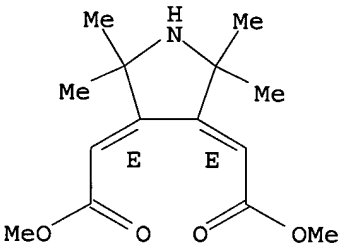
RN 108086-63-1 HCAPLUS
CN Acetic acid, 2,2'-(2,2,5,5-tetramethyl-3,4-pyrrolidinediylidene)bis-, dimethyl ester, (E,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 108086-64-2 HCAPLUS
CN Acetic acid, 2,2'-(2,2,5,5-tetramethyl-3,4-pyrrolidinediylidene)bis-, dimethyl ester, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L8 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:408884 HCAPLUS
DOCUMENT NUMBER: 59:8884
ORIGINAL REFERENCE NO.: 59:1594c-h,1595a-g
TITLE: Pyrrolidine derivatives
PATENT ASSIGNEE(S): Parke, Davis, & Co.
SOURCE: 20 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 619108		19621015	BE	
FR 1337793			FR	

FR M2518		FR		
FR M2519		FR		
FR M2520		FR		
FR M2521		FR		
GB 1002851		GB		
US 3149123	19640915	US 1962-197935	19620528	
PRIORITY APPLN. INFO.:		GB	19610104	

GI For diagram(s), see printed CA Issue.

AB I, where R is H, lower alkyl, or lower acyl, R1 is Pr, and R2, R3 are H or Me, were prepared I and their salts with pharmaceutically acceptable organic and inorg. acids displayed interesting analgesic activity. I, where R is H or lower alkyl radical and R2 = R3 = H, can be prepared by reduction of the corresponding succinimide with a complex metallic hydride in an anhydrous inert solvent. Thus, a solution of 46.5 g. N-methyl-α-(m-methoxyphenyl)-α-propylsuccinimide (II) in 200 mL. Et2O was added dropwise with stirring to 10 g. LiAlH4 in 200 mL. Et2O. The mixture was refluxed and stirred 2 h., cooled, treated with 30 mL. H2O, filtered, concentrated, and distilled in vacuo to give 1-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (III), b. 119-21°; HCl salt m. 133-5° (iso-PrOH-Et2O). The HBr salt was prepared by treatment of an ethereal solution of III with 1 equivalent HBr. Similarly, the citrate was prepared from III and 1 equivalent of citric acid in iso-PrOH by removal of solvent in vacuo. II was prepared by adding 30.3 g. KCN to 96.5 g. Et α-cyano-β-(m-methoxyphenyl)-β-propylacrylate in 150 mL. aqueous EtOH. The mixture was heated for 30 min. on a steam bath, cooled, acidified, and extracted with Et2O. The crude Et α,β-dicyano-β-(m-methoxyphenyl)-hexanoate thus obtained was refluxed 80 h. with 0.5 l. concentrated HCl, extracted with Et2O, the Et2O removed in vacuo, and the α-(m-methoxyphenyl)-α-propylsuccinic acid obtained as an oil. To 81.6 g. of the last, 32 g. of 40% aqueous MeNH2 was added and the mixture gradually heated, kept 1 h. at 190°, and distilled in vacuo to give II, b0.6 167-74°, n20D 1.5475. III (21.4 g.) was refluxed 90 min. with 90 mL. azeotropic HBr and concentrated in vacuo. The product was dissolved in 100 mL. H2O, made basic with NaHCO3, extracted with Et2O, and the Et2O removed to give I (R1 = R2 = R3H, R1 = Pr) (IV); HCl salt m. 145-6° (iso-PrOH-Et2O). A mixture of 9.6 g. I (R1 = Pr, R = R2 = Me, R3 = H) and 30 mL. azeotropic HBr was refluxed 2 h., evaporated to dryness, dissolved in H2O, made basic with K2CO3, and extracted with CHCl3 to give I (R1 = Pr, R = R3 = H,R2 = Me). Similarly, I(R1 = Pr, R = R2 = H,R3 = Me),b0.7 147-50°, was obtained. A mixture of 30 mL. Ac2O, 10 mL. pyridine, and 8.1 g. IV was heated 2 h. at 90°, concentrated, and the residue distilled in vacuo to give I (R = Ac, R2 = R3 = H, R1 = Pr) (V), b0.7 136-8°, n20D 1.5228. By using the d- or l-isomer of IV in the above process, the corresponding d-V (b11 138-9°, [α]24D 18.4°) or l-V (b0.6 129°, [α]20D -19.2°) was obtained. Similarly, I(R = EtCO, R1, = Pr, R2 = Me, R3 = H) was prepared from (EtCO)2O and I (R = R3 = H, R1 = Pr, R2 =Me), and I (R = Ac, R1 = Pr, R2 = H, R3 = Me) (b0.9 132°, n20D 1.5104), from Ac2O and I (R = R2 = H, R1 = Pr, R3 =Me). To 4.3 g. 5-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (VI), 5 mL. HCO2H was added, followed by 50 mL. of 40% aqueous HCHO. The mixture was heated 6 h. at 95°, poured into 50 mL. H2O, made basic with K2CO2, and extracted with Et2O to give I (R =R3 = Me, R1 = Pr, R2 = H),b0.4 114-18°,n20D 1.5156. VI was prepared by adding dropwise with stirring 140 g. α-(m-methoxyphenyl)valeronitrile to 29 g. NaNH2 in 350 mL. anhydrous Et2O. The red solution was refluxed 3 h. under N, cooled, treated with 50 g. 1,2-propylene oxide, refluxed 3 addnl. hrs., cooled, 100 mL. H2O added,

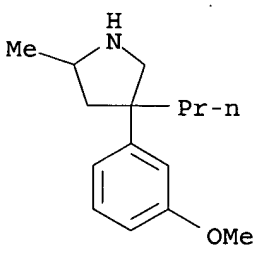
and the ethereal phase separated and washed to give 4-cyano-4-(m-methoxyphenyl)-2-heptanol (VII), b0.7 143-7°, n20D 1.5280. VII (100 g.) was added dropwise to 23 g. LiAlH4 in 500 mL. Et2O, the solution refluxed 4 h., treated successively with 15 mL. H2O, 15 mL. aqueous 4N NaOH, and 45 mL. H2O, refluxed 1 h., filtered, concentrated, and distilled in vacuo to give 4-aminomethyl-4-(m-methoxyphenyl)-2-heptanol (VIII), b0.7 153-8°, n20D 1.5310. A solution of 70 g. VIII in 250 mL. CHCl3 was saturated with HCl, cooled to 0°, and treated with 66 g. SOCl2. The mixture was slowly heated and boiled 3 h., then concentrated in vacuo, treated with 200 mL. H2O, made strongly basic with Na2CO3, heated 2 h. at 95°, cooled, and extracted with EtO. After removal of Et2O, the residue was distilled in vacuo to give VI, b0.4 123-6°, n20D 1.5310. Similarly, III (b1 119-21°) was prepared from 3-(m-methoxyphenyl)-3-propylpyrrolidine (IX), HCO2H, and HCHO. To prepare IX, 44.5 g. PhCH2NH2 was added to 81.6 g. α-(m-methoxyphenyl)-α-propylsuccinic acid and the mixture was gradually brought to 190° and heated 1 h. The product was distilled in vacuo to furnish the oily N-benzyl-α-(m-methoxyphenyl)-α-propylsuccinimide (X). X was converted to N-benzyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (XI) (b0.7 182-6°, n20D 1.3604) by reduction with LiAlH4 in Et2O. Upon catalytic hydrogenation in EtOH (5% Pd-C, 1 atmospheric H), the benzyl group was removed to yield IX, b0.8 125-9°, n20D 1.5388. IX was also prepared by reduction of 2-(2-chloroethyl)-2-(m-methoxyphenyl)valeronitrile with LiAlH4 in Et2O. To a solution of 9.8 g. IX in 50 mL. HCONMe2, 12 g. Na2CO3 was added, followed by 4.3 g. MeI. The mixture was stirred and mildly heated for 5 h., cooled, poured into H2O, and the obtained solution was extracted with Et2O. After removal of Et2O, the residue was distilled in vacuo to furnish III. A suspension of 5 g. 1,2-dimethyl-3-(m-methoxyphenyl)-3-propyl-1-pyrrolinium iodide (XII) in 125 mL. Bu2O was added dropwise to 1 g. LiAlH4 in 25 mL. Bu2O, the mixture refluxed 1 h., cooled, treated with 3 mL. H2O, filtered, concentrated, and distilled in vacuo to give 1,2-dimethyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (b1.8 142-4°, n20D 1.5224). XII was prepared by slow addition of 582 g. m-methoxybenzyl cyanide to 155 g. NaNH2 in 3 l. C6H6 below 5°. The red solution was stirred 2 h. at that temperature, 525 g. PrBr added, the solution brought to room temperature, gradually heated, boiled 3 h., cooled, treated with 1 l. H2O, neutralized with 2N H2SO4, and the C6H6 layer was separated, washed with H2O, concentrated, and distilled to give α-(m-methoxyphenyl)valeronitrile (XIII), b0.4 112-20°, n20D 1.5150. XIII (330 g.) was added with stirring to NaNH2 (71 g.) in C6H6 (2 l.) at a temperature <10°, the red mixture was boiled 2 h., cooled to 5°, treated with 350 g. (CH2Cl)2 in 20 min. at 5°, stirred 2 h. at 5°, then slowly heated, boiled 6 h., cooled, treated with 0.5 l. H2O, and neutralized with 2N H2SO4. The C6H6 layer was separated, washed with H2O, concentrated, and distilled in vacuo to give 3-cyano-3-(m-methoxyphenyl)-1-chlorohexane (XIV), b0.5 133-5°, n20D 1.5221. A solution of MeMgBr (prepared from 20 g. Mg and 80 g. MeBr) in 200 mL. Bu2O was freed from excess MeBr by partial distillation, then treated with 52.5 g. XIV in 200 mL. Bu2O. The mixture was heated 3 h. at 120°, cooled, treated with a saturated solution of NH4Cl, and stirred 10 min. The aqueous phase was separated and washed with CHCl3. The organic phases were combined, concentrated under vacuum, the oily residue was extracted 4 times with cold 2N HCl, the exts. were made basic, and extracted with Et2O to furnish crude 2-methyl-3-(m-methoxyphenyl)-3-propyl-1-pyrroline (XV). To a solution of 10 g. XV in 50 mL. HCONMe2, 4.5 g. MeI was added, the mixture was stirred and

heated 5 h., cooled, evaporated to dryness, and the residue triturated with Et2O to give XII, m. 147-80 (CHCl3Et2O). XV was reduced to 2-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (XVI) (b0.6 129°, n20D 1.5330) with LiAlH4 in Bu2O. XVI can be methylated with HCO2H and HCHO or with MeI to give I (R = R2 = Me, R1 = Pr, R3 = H). To a solution of 5 g. dl-III in 70 mL. hot iso-PrOH, a solution of 9 g. (-)-di-p-toluoyl-L-(+)-tartaric acid in 70 mL. hot iso-PrOH was added. After cooling, the (-)-di-p-toluoy-L-(+)-tartrate of l-III was obtained, m. 134° (iso-PrOH), [α]21.5D -90°. A solution of 5.35 g. of the latter was made basic with aqueous NaOH, extracted with Et2O, the extract dried, evaporated, and distilled in vacuo to give l-III, b1 120°, [α]21.5D -19.8°. By treatment of the iso-PrOH mother liquor with (+)-di-p-toluoyl-D(-)-tartaric acid, the (+)-di-p-toluoyl-D-(-)-tartrate of d-III was obtained [m. 134° (iso-PrOH), [α]26D 89.7°], which was similarly transformed to the free base d-III (b0.9 120°, [α]26D 16.5°). From l-III, l-1-methyl-3-(m-hydroxyphenyl)-3-propylpyrrolidine (l-XVII) was obtained, by treatment with azeotropic HBr; HCl salt m. 145-7° (iso-PrOH-Et2O), [α]26D 11.3° (c 0.85, EtOH). Similarly, d-III led to the hydrochloride of d-XVII, m. 142-5°, [α]25D 14.8° (c 0.9, EtOH).

IT 1507-71-7P, Pyrrolidine, 3-(m-methoxyphenyl)-5-methyl-3-propyl-
1507-75-1P, Pyrrolidine, 3-(m-methoxyphenyl)-2-methyl-3-propyl-
RL: PREP (Preparation)
(preparation of)

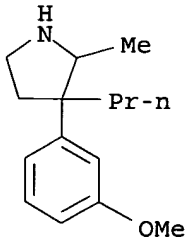
RN 1507-71-7 HCAPLUS

CN Pyrrolidine, 4-(m-methoxyphenyl)-2-methyl-4-propyl- (7CI, 8CI) (CA INDEX NAME)



RN 1507-75-1 HCAPLUS

CN Pyrrolidine, 3-(m-methoxyphenyl)-2-methyl-3-propyl- (7CI, 8CI) (CA INDEX NAME)



L8 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN

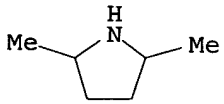
ACCESSION NUMBER: 1924:22514 HCAPLUS
DOCUMENT NUMBER: 18:22514
ORIGINAL REFERENCE NO.: 18:3055b-i
TITLE: Diazo coupling of methylene bases
AUTHOR(S): Konig, W.
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1924), 57B, 891-5
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. Rosenhauer, Z. angew. Chemical 37, 152. A continuation of the study of the diazo coupling of methylene bases (cf. C. A. 18, 2163) has shown that the conditions described in the earlier papers (treatment of the methylcyclammonium iodides in aqueous NaOH or Na2CO3) lead to complications; the quaternary iodides, even in the presence of an excess of alkali, convert the diazo compds. to a not inconsiderable extent into PhI derivs. which cling tenaciously to the azo dyes formed as the chief product. Moreover, in the coupling especially of diazotized p-O2NC6H4NH2 with the methylene bases of the quinoline and benzothiazole series there are always formed, in addition to the monoazo dyes, some of which have already been described, varying amts. of other dye salts, which are very difficult to sep. and very similar in appearance to the former, although somewhat more easily hydrolyzed, and which in concentrated H2SO4 show pure blue and not red onium halochromism. Furthermore, spectroscopic examination having shown that the nature of the alkyl on the N of the methylene base has so little influence on the maximum of absorption of light by the corresponding azo dye that the readings fall within the exptl. error, the suspicion arose that the compds. described in the earlier papers were not quite pure and that they did not have the structure I but II (Y = -CH:CH-, -S-, -ClAk2-, etc.). To test this point N,β,β-trimethyl-α-methyleneindoline was coupled with diazotized p-IC6H4NH2, an especially careful process of preparation and purification being used to insure homogeneity of the coupling product. The Cu-colored salt (III) so obtained gave on microanalysis results showing beyond doubt that it has the structure II (Y = CMe2, Ar = p-IC6H4, Alk = Me, X = ClO4), the presence of Me on the N being confirmed by analysis of the light cinnabar-red free base which is soluble in organic solvents with pure green-yellow color, i. e., without "basochromism." Macroanalysis of the product obtained from Fischer's base and diazotized p-O2NC6H4NH2 had already shown that it contains more C and H than calculated for the Me-free derivative and that it is therefore a 1,3,3-trimethyl-2-[4'-nitrobenzeneazomethylene]-indoline. 1,3,3-Trimethyl-2-[4'-iodobenzeneazomethylene]indoline perchlorate (III), from 2.8 g. of the perchlorate of Fischer's base in cold C5H5N slowly treated with 10% Na2CO3 and diazotized p-IC6H4NH2, decomps. above 270°, soluble in hot H2O with yellow, in concentrated H2SO4 with yellow-green color changing to blue-green and, on dilution with H2O, to orange, dyes tannated cotton from H2O a clear golden yellow (about shade 17 on the Ostwald scale when 1% of dye is used); free base, m. 183°; HCl salt, CrO3-like needles, m. about 226°. When 14 g. quinaldine-Me2SO4 is similarly treated with diazotized p-O2NC6H4NH2 there is obtained a black-violet color base converted by HCl into a mixture of 2 chlorides, separated by repeated extraction with insufficient amts. of boiling H2O; one (formed in smaller amount) remains undissolved as a brown-violet powder soluble in concentrated H2SO4 with pure blue color (bands at about 637 and 588μμ), which was not obtained quite pure; the other is obtained from the yellow aqueous extract by repeated precipitation

from H2O with NaCl and crystallization from AcOH saturated with HCl in orange needles
with bluish shimmer, m. about 240°, soluble in concentrated H2SO4 with pure red color (band at about 527μμ), whose composition agrees well with that calculated for the N-Me compound (II, Y = CH:CH, Ar = p-O2NC6H4, Alk = Me, X = Cl); the free base, violet-black needles with bronze luster, m. 190° (formerly given as 171°), is probably identical with a base m. 186° obtained by Rosenhauer from ω-bromoquinaldine-MeBr and p-O2NC6H4NHNH2 and therefore also has a structure analogous to II instead of the one previously assigned to it.

IT 3378-71-0P, Pyrrolidine, 2,5-dimethyl-
RL: PREP (Preparation)
(preparation of)

RN 3378-71-0 HCAPLUS

CN Pyrrolidine, 2,5-dimethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



=> d l10 ibib abs hitstr tot

L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1963:408884 HCAPLUS
DOCUMENT NUMBER:	59:8884
ORIGINAL REFERENCE NO.:	59:1594c-h,1595a-g
TITLE:	Pyrrolidine derivatives
PATENT ASSIGNEE(S):	Parke, Davis, & Co.
SOURCE:	20 pp.
DOCUMENT TYPE:	Patent
LANGUAGE:	Unavailable
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 619108		19621015	BE	
FR 1337793			FR	
FR M2518			FR	
FR M2519			FR	
FR M2520			FR	
FR M2521			FR	
GB 1002851			GB	
US 3149123		19640915	US 1962-197935	19620528
PRIORITY APPLN. INFO.:			GB	19610104

GI For diagram(s), see printed CA Issue.

AB I, where R is H, lower alkyl, or lower acyl, R1 is Pr, and R2, R3 are H or Me, were prepared I and their salts with pharmaceutically acceptable organic and inorg. acids displayed interesting analgesic activity. I, where R is H or lower alkyl radical and R2 = R3 = H, can be prepared by reduction of the corresponding succinimide with a complex metallic hydride in an anhydrous inert solvent. Thus, a solution of 46.5 g. N-methyl-α-(m-methoxyphenyl)-α-propylsuccinimide (II) in 200 mL. Et2O was added dropwise with stirring to 10 g. LiAlH4 in 200 mL. Et2O. The mixture was refluxed and stirred 2 h., cooled, treated with 30 mL. H2O, filtered,

concentrated, and distilled in vacuo to give 1-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (III), b. 119-21°; HCl salt m. 133-5° (iso-PrOH-Et2O). The HBr salt was prepared by treatment of an ethereal solution of III with 1 equivalent HBr. Similarly, the citrate was prepared from III and 1 equivalent of citric acid in iso-PrOH by removal of solvent in vacuo. II was prepared by adding 30.3 g. KCN to 96.5 g. Et α-cyano-β-(m-methoxyphenyl)-β-propylacrylate in 150 mL. aqueous EtOH. The mixture was heated for 30 min. on a steam bath, cooled, acidified, and extracted with Et2O. The crude Et α,β-dicyano-β-(m-methoxyphenyl)-hexanoate thus obtained was refluxed 80 h. with 0.5 l. concentrated HCl, extracted with Et2O, the Et2O removed in vacuo, and the α-(m-methoxyphenyl)-α-propylsuccinic acid obtained as an oil. To 81.6 g. of the last, 32 g. of 40% aqueous MeNH2 was added and the mixture gradually heated, kept 1 h. at 190°, and distilled in vacuo to give II, b0.6 167-74°, n20D 1.5475. III (21.4 g.) was refluxed 90 min. with 90 mL. azeotropic HBr and concentrated in vacuo. The product was dissolved in 100 mL. H2O, made basic with NaHCO3, extracted with Et2O, and the Et2O removed to give I (R1 = R2 = R3H, R1 = Pr) (IV); HCl salt m. 145-6° (iso-PrOH-Et2O). A mixture of 9.6 g. I (R1 = Pr, R = R2 = Me, R3 = H) and 30 mL. azeotropic HBr was refluxed 2 h., evaporated to dryness, dissolved in H2O, made basic with K2CO3, and extracted with CHCl3 to give I (R1 = Pr, R = R3 = H,R2 = Me). Similarly, I(R1 = Pr, R = R2 = H,R3 = Me),b0.7 147-50°, was obtained. A mixture of 30 mL. Ac2O, 10 mL. pyridine, and 8.1 g. IV was heated 2 h. at 90°, concentrated, and the residue distilled in vacuo to give I (R = Ac, R2 = R3 = H, R1 = Pr) (V), b0.7 136-8°, n20D 1.5228. By using the d- or l-isomer of IV in the above process, the corresponding d-V (b11 138-9°, [α]24D 18.4°) or l-V (b0.6 129°, [α]20D -19.2°) was obtained. Similarly, I(R = EtCO, R1, = Pr, R2 = Me, R3 = H) was prepared from (EtCO)2O and I (R = R3 = H, R1 = Pr, R2 =Me), and I (R = Ac, R1 = Pr, R2 = H, R3 = Me) (b0.9 132°, n20D 1.5104), from Ac2O and I (R = R2 = H, R1 = Pr, R3 =Me). To 4.3 g. 5-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (VI), 5 mL. HCO2H was added, followed by 50 mL. of 40% aqueous HCHO. The mixture was heated 6 h. at 95°, poured into 50 mL. H2O, made basic with K2CO2, and extracted with Et2O to give I (R =R3 = Me, R1 = Pr, R2 = H),b0.4 114-18°,n20D 1.5156. VI was prepared by adding dropwise with stirring 140 g. α-(m-methoxyphenyl)valeronitrile to 29 g. NaNH2 in 350 mL. anhydrous Et2O. The red solution was refluxed 3 h. under N, cooled, treated with 50 g. 1,2-propylene oxide, refluxed 3 addnl. hrs., cooled, 100 mL. H2O added, and the ethereal phase separated and washed to give 4-cyano-4-(m-methoxyphenyl)-2-heptanol (VII), b0.7 143-7°, n20D 1.5280. VII (100 g.) was added dropwise to 23 g. LiAlH4 in 500 mL. Et2O, the solution refluxed 4 h., treated successively with 15 mL. H2O, 15 mL. aqueous 4N NaOH, and 45 mL. H2O, refluxed 1 h., filtered, concentrated, and distilled in vacuo to give 4-aminomethyl-4-(m-methoxyphenyl)-2-heptanol (VIII), b0.7 153-8°, n20D 1.5310. A solution of 70 g. VIII in 250 mL. CHCl3 was saturated with HCl, cooled to 0°, and treated with 66 g. SOCl2. The mixture was slowly heated and boiled 3 h., then concentrated in vacuo, treated with 200 mL. H2O, made strongly basic with Na2CO3, heated 2 h. at 95°, cooled, and extracted with EtO. After removal of Et2O, the residue was distilled in vacuo to give VI, b0.4 123-6°, n20D 1.5310. Similarly, III (b1 119-21°) was prepared from 3-(m-methoxyphenyl)-3-propylpyrrolidine (IX), HCO2H, and HCHO. To prepare IX, 44.5 g. PhCH2NH2 was added to 81.6 g. α-(m-methoxyphenyl)-α-propylsuccinic acid and the mixture was gradually brought to 190° and heated 1 h. The

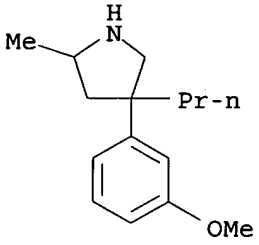
product was distilled in vacuo to furnish the oily N-benzyl-α-(m-methoxyphenyl)-α-propylsuccinimide (X). X was converted to N-benzyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (XI) (b0.7 182-6°, n20D 1.3604) by reduction with LiAlH4 in Et2O. Upon catalytic hydrogenation in EtOH (5% Pd-C, 1 atmospheric H), the benzyl group was removed to yield IX, b0.8 125-9°, n20D 1.5388. IX was also prepared by reduction of 2-(2-chloroethyl)-2-(m-methoxyphenyl)valeronitrile with LiAlH4 in Et2O. To a solution of 9.8 g. IX in 50 mL. HCONMe2, 12 g. Na2CO3 was added, followed by 4.3 g. MeI. The mixture was stirred and mildly heated for 5 h., cooled, poured into H2O, and the obtained solution was extracted with Et2O. After removal of Et2O, the residue was distilled in vacuo to furnish III. A suspension of 5 g. 1,2-dimethyl-3-(m-methoxyphenyl)-3-propyl-1-pyrrolinium iodide (XII) in 125 mL. Bu2O was added dropwise to 1 g. LiAlH4 in 25 mL. Bu2O, the mixture refluxed 1 h., cooled, treated with 3 mL. H2O, filtered, concentrated, and distilled in vacuo to give 1,2-dimethyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (b1.8 142-4°, n20D 1.5224). XII was prepared by slow addition of 582 g. m-methoxybenzyl cyanide to 155 g. NaNH2 in 3 l. C6H6 below 5°. The red solution was stirred 2 h. at that temperature, 525 g. PrBr added, the solution brought to room temperature, gradually heated, boiled 3 h., cooled, treated with 1 l. H2O, neutralized with 2N H2SO4, and the C6H6 layer was separated, washed with H2O, concentrated, and distilled to give α-(m-methoxyphenyl)valeronitrile (XIII), b0.4 112-20°, n20D 1.5150. XIII (330 g.) was added with stirring to NaNH2 (71 g.) in C6H6 (2 l.) at a temperature <10°, the red mixture was boiled 2 h., cooled to 5°, treated with 350 g. (CH2Cl)2 in 20 min. at 5°, stirred 2 h. at 5°, then slowly heated, boiled 6 h., cooled, treated with 0.5 l. H2O, and neutralized with 2N H2SO4. The C6H6 layer was separated, washed with H2O, concentrated, and distilled in vacuo to give 3-cyano-3-(m-methoxyphenyl)-1-chlorohexane (XIV), b0.5 133-5°, n20D 1.5221. A solution of MeMgBr (prepared from 20 g. Mg and 80 g. MeBr) in 200 mL. Bu2O was freed from excess MeBr by partial distillation, then treated with 52.5 g. XIV in 200 mL. Bu2O. The mixture was heated 3 h. at 120°, cooled, treated with a saturated solution of NH4Cl, and stirred 10 min. The aqueous phase was separated and washed with CHCl3. The organic phases were combined, concentrated under vacuum, the oily residue was extracted 4 times with cold 2N HCl, the exts. were made basic, and extracted with Et2O to furnish crude 2-methyl-3-(m-methoxyphenyl)-3-propyl-1-pyrroline (XV). To a solution of 10 g. XV in 50 mL. HCONMe2, 4.5 g. MeI was added, the mixture was stirred and heated 5 h., cooled, evaporated to dryness, and the residue triturated with Et2O to give XII, m. 147-80 (CHCl3Et2O). XV was reduced to 2-methyl-3-(m-methoxyphenyl)-3-propylpyrrolidine (XVI) (b0.6 129°, n20D 1.5330) with LiAlH4 in Bu2O. XVI can be methylated with HCO2H and HCHO or with MeI to give I (R = R2 = Me, R1 = Pr, R3 = H). To a solution of 5 g. dl-III in 70 mL. hot iso-PrOH, a solution of 9 g. (-)-di-p-toluoyl-L-(+)-tartaric acid in 70 mL. hot iso-PrOH was added. After cooling, the (-)-di-p-toluoy-L-(+)-tartrate of l-III was obtained, m. 134° (iso-PrOH), [α]21.5D -90°. A solution of 5.35 g. of the latter was made basic with aqueous NaOH, extracted with Et2O, the extract dried, evaporated, and distilled in vacuo to give l-III, b1 120°, [α]21.5D -19.8°. By treatment of the iso-PrOH mother liquor with (+)-di-p-toluoyl-D(-)-tartaric acid, the (+)-di-p-toluoyl-D-(-)-tartrate of d-III was obtained [m. 134° (iso-PrOH), [α]26D 89.7°], which was similarly transformed to the free base d-III (b0.9 120°, [α]26D 16.5°). From l-III, l-1-methyl-3-(m-hydroxyphenyl)-3-propylpyrrolidine (l-XVII) was obtained,

by treatment with azeotropic HBr; HCl salt m. 145-7° (iso-PrOH-Et2O), [α]26D 11.3° (c 0.85, EtOH). Similarly, d-III led to the hydrochloride of d-XVII, m. 142-5°, [α]25D 14.8° (c 0.9, EtOH).

IT 1507-71-7P, Pyrrolidine, 3-(m-methoxyphenyl)-5-methyl-3-propyl-
1507-75-1P, Pyrrolidine, 3-(m-methoxyphenyl)-2-methyl-3-propyl-
RL: PREP (Preparation)
(preparation of)

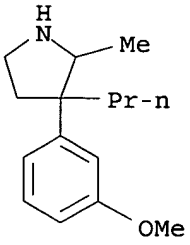
RN 1507-71-7 HCAPLUS

CN Pyrrolidine, 4-(m-methoxyphenyl)-2-methyl-4-propyl- (7CI, 8CI) (CA INDEX NAME)



RN 1507-75-1 HCAPLUS

CN Pyrrolidine, 3-(m-methoxyphenyl)-2-methyl-3-propyl- (7CI, 8CI) (CA INDEX NAME)



=> d l17 ibib abs hitstr tot

L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:722955 HCAPLUS

DOCUMENT NUMBER: 141:243334

TITLE: An efficient and cost-effective process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol

INVENTOR(S): Ku, Yi-yin; Cowart, Marlon D.; Sharma, Padam N.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004171845	A1	20040902	US 2003-376534	20030227
CA 2515801	A1	20040910	CA 2004-2515801	20040225
WO 2004076388	A2	20040910	WO 2004-US5573	20040225
WO 2004076388	A3	20041202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1601650	A2	20051207	EP 2004-714598	20040225

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2006519233	T	20060824	JP 2006-503863	20040225
PRIORITY APPLN. INFO.:			US 2003-376534	A 20030227
			WO 2004-US5573	W 20040225

OTHER SOURCE(S): MARPAT 141:243334

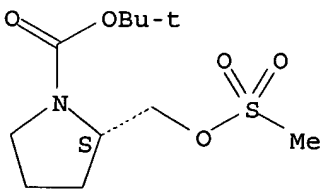
AB The invention relates to an efficient and cost-effective process for preparing 2-methylpyrrolidine and, more particularly, specific enantiomers of 2-methylpyrrolidine, from (R/S)-prolinol. Novel intermediates also are described. The title compds. were synthesized in several steps via N-protection of corresponding chiral prolinols, conversion of the hydroxy groups to sulfonates or iodides, reduction and finally N-deprotection. The iodides could also be prepared from the corresponding sulfonates via reaction with metal iodides . Thus, (S)-prolinol was N-protected with tert-butoxycarbonyl anhydride (100% yield) followed by sulfonylation with mesyl chloride (96% yield). The resulting mesylate was either directly reduced to (R)-N-Boc-2-methylpyrrolidine with lithium triethoxyborohydride (54% yield) or via the iodide intermediate through iodination with LiI (79% yield) followed by hydrogenolysis in the presence of Pd/C (85.9% yield). (R)-N-Boc-2-methylpyrrolidine was then deprotected with HCl to give 2-(R)-methylpyrrolidine hydrochloride (96% yield).

IT 132482-09-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol)

RN 132482-09-8 HCAPLUS

CN 1-Pyrrolidinecarboxylic acid, 2-[[(methylsulfonyl)oxy]methyl]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d l15 ibib abs tot

L15 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:919436 HCAPLUS
DOCUMENT NUMBER: 145:315009
TITLE: Preparation of bicyclic heterocycles, particularly pyrimido[2,1-c][1,4]oxazine-2-carboxamides, as HIV integrase inhibitors
INVENTOR(S): Naidu, B. Narasimhulu; Banville, Jacques; Beaulieu, Francis; Connolly, Timothy P.; Krystal, Mark R.; Matiskella, John D.; Ouellet, Carl; Plamondon, Serge; Remillard, Roger; Sorenson, Margaret E.; Ueda, Yasutsugu; Walker, Michael A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 182 pp., Cont.-in-part of U.S. Ser. No. 126,891.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

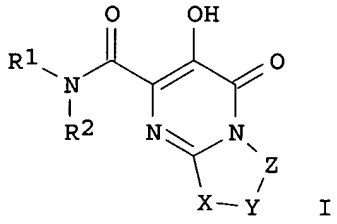
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006199956	A1	20060907	US 2005-288533	20051129
US 7157447	B2	20070102		
US 2005267105	A1	20051201	US 2005-126891	20050511
US 7176196	B2	20070213		
WO 2005118589	A1	20051215	WO 2005-US18567	20050527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005118590	A1	20051215	WO 2005-US18568	20050527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1749008	A1	20070207	EP 2005-758639	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV, MK, YU				
EP 1753767	A1	20070221	EP 2005-754152	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV, MK, YU				

PRIORITY APPLN. INFO.:

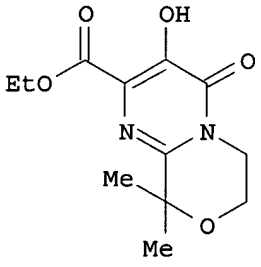
US 2004-575513P	P	20040528
US 2004-603371P	P	20040820
US 2005-126891	A2	20050511
US 2005-138726	A	20050526
US 2005-138773	A	20050526
WO 2005-US18567	W	20050527
WO 2005-US18568	W	20050527

OTHER SOURCE(S): MARPAT 145:315009

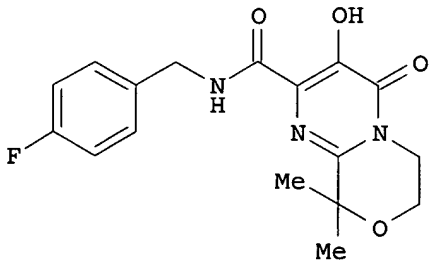
GI



I



II



III

AB The invention is related to the preparation of title compds. I [R1 = C1-6(Ar1)alkyl, C1-6(Ar1)oxyalkyl, C1-6(Ar1)hydroxyalkyl, etc.; R2 = H, alkyl, OH, alkyloxy; Ar1 = (un)substituted Ph, naphthyl, benzothiophenyl, etc.; X-Y-Z = C(R3)2OC(R3)2, C(R3)2OC(R3)2C(R3)2, C(R3)2C(R3)2C(R3)2C(R3)2; R3 = H, alkyl], and their pharmaceutically acceptable salts or solvates which inhibit HIV integrase and prevent viral integration into human DNA. The invention is also related to the pharmaceutical compns. comprising pyrimidinones I, and methods of using them for treating HIV infection and AIDS. Thus, reacting ester II (preparation given) with 4-fluorobenzylamine in DMF/ethanol in the presence of TEA at 90° gave amide III in 82% yield. Selected I displayed IC50 values in the range of 0.002-0.1 μM for the inhibition of HIV integrase activity. III demonstrated synergistic or additive-synergistic HIV antiviral activity when used in combination with other antiviral agents, e.g., zidovudine, indinavir, T-20, etc.

L15 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:190690 HCAPLUS

DOCUMENT NUMBER: 144:274258

TITLE: Preparation of 2-arylaminobenzoxazole derivatives as inhibitors of very late antigen-4 (VLA-4)

INVENTOR(S): Chiba, Atsushi; Machinaga, Nobuo; Iimura, Makoto; Muro, Fumito; Ootori, Hideko

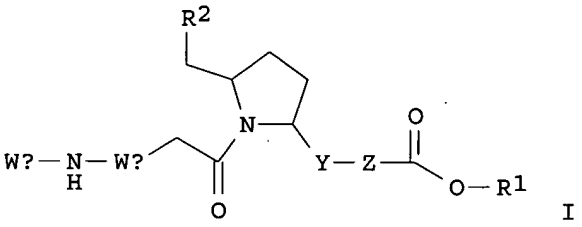
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 145 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006056830	A	20060302	JP 2004-240570	20040820
PRIORITY APPLN. INFO.:			JP 2004-240570	20040820

OTHER SOURCE(S): MARPAT 144:274258
GI



I

AB The title compds. (I) [Wa = each (un)substituted aryl or heteroaryl; Wb = each (un)substituted 1,3-benzoxazole or 1,3-benzothiazole ring divalent group; R1 = H, lower alkyl; R2 = NR3R4; wherein R3, R4 = H, HO, each (un)substituted lower alkyl, cycloalkyl, lower alkoxy,or cycloalkyloxy; or NR3R4 together forms (un)substituted 4- to 7-membered heterocyclic ring; Y = (CH2)n-O; n = 1,2; Z = cyclohexane ring] or salts thereof or solvates of either are prepared These compds. are potent inhibitors of VLA-4 and excellent in water solubility and small intestine membrane permeability, effective through oral administration, and highly safe. They are useful for the prevention and/or treatment of diseases caused by cell adhesion related to VLA-4 including inflammation, autoimmune diseases, cancer metastasis, bronchial asthma, nasal obstruction, diabetes, arthritis, psoriasis, multiple sclerosis, inflammatory bowel diseases, and transplant rejection. Thus, trans-4-[(5S)-(4-morpholinyl)methyl-(2S)-pyrrolidinylmethoxy]cyclohexanecarboxylic acid Et ester hydrochloride was condensed with [7-fluoro-2-[(5-fluoro-2-methylphenyl)amino]-6-benzoxazolyl]acetic acid using HOBt, EDC, and Et3N at room temperature overnight (80% yield) followed by saponification with NaOH in aqueous MeOH and acidification with 1 N aqueous HCl solution to give 69% trans-4-[1-[[7-fluoro-2-(2-methylphenylamino)-6-benzoxazolyl]acetyl]-(5S)-(4-morpholinyl)methyl-(2S)-pyrrolidinylmethoxy]cyclohexanecarboxylic acid (II). II in vitro inhibited the binding of Eu3+-DID7-IgG to 4B4 cells (CHO K1 cells expressing VLA-4 mols.) with IC50 of 0.6 μg/mL.

L15 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:165657 HCAPLUS
DOCUMENT NUMBER: 144:233060
TITLE: Preparation of 2-aryloxazole derivatives as histamine H3 receptor agents
INVENTOR(S): Beavers, Lisa Selsam; Boulet, Serge Louis; Finn, Terry Patrick; Gadski, Robert Alan; Hornback, William Joseph; Jesudason, Cynthia Darshini; Pickard, Richard Todd; Stevens, Freddie Craig; Vaught, Grant Matthews

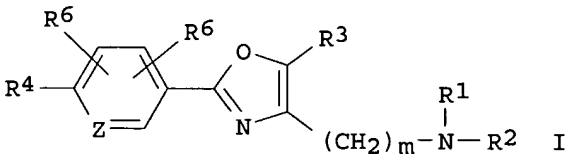
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006019833	A1	20060223	WO 2005-US24883	20050714

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-591191P P 20040726
OTHER SOURCE(S): MARPAT 144:233060
GI



I

AB Aryloxazole compds. (I), or pharmaceutically acceptable salts thereof [m = independently at each occurrence 1, 2, or 3, wherein optionally one or two of the hydrogens of the CH2, CH2CH2, or CH2CH2CH2 so formed may independently be replaced by halogen, or optionally on a carbon not adjacent to nitrogen one of the hydrogens of the CH2CH2, or CH2CH2CH2 so formed may independently be replaced by OH or each (un)substituted O-(C1-C4) alkyl or -(C1-C3)alkyl; Z = carbon (substituted with hydrogen or the optional substituents indicated herein) or nitrogen, provided that when Z = nitrogen then R6 is not attached to Z; R1, R2 = C1-7 alkyl (optionally substituted with one to three halogens), or NR1R2 forms each optionally substituted azetidinyl, pyrrolidinyl, piperidinyl ring; R3 = H, halogen, each (un)substituted C1-4 alkyl or C1-4 alkoxy; R4 = halogen, (un)substituted C1-7 alkyl, cyano, C(O)R7, (un)substituted C(O)C3-7 cycloalkyl, C(O)NR7R8, OR7, -O-phenyl-(R10)(R11), NO2, NR7R8, NR7SO2-R7, NR7C(O)R7, NR7CO2R7, NR7C(O)NR7R8, SR7, SO2R7, SO2NR7R8, S(O)R7, O(CH2)mNR7R8, heteroaryl-R9, OCH2-heteroaryl-R9, etc.; R6 = H, halogen, Me; R7, R8 = H, or (un)substituted C1-7 alkyl; or NR7R8 forms a four to seven membered ring; R9 = H, cyano, (un)substituted C1-3 alkyl; R10-R12 = H, halogen, (un)substituted C1-7 alkyl, hydroxy-C1-7 alkyl, cyano, etc.] are prepared These compds. have histamine-H3 receptor antagonist or inverse agonist activity and are used to treat obesity, cognitive deficiencies, narcolepsy, and other histamine H3 receptor-related diseases. Thus, 2-(4-bromophenyl)-4-[(pyrrolidin-1-yl)methyl]oxazole hydrochloride 0.151,

4-methylsulfonylphenylboronic acid 0.132, tetrakis(triphenylphosphine)pall adium 0.010 g, aqueous Na2CO3 (2M, 0.88 mL) and 7 mL dioxane were placed in a 10 mL CEM microwave tube. The tube was placed in a CEM microwave reactor for 30 min at 90°, 25 psi, and 45 W of power to give, after silica gel chromatog., 0.125 g 2-[4'-(methylsulfonyl)biphenyl-4-yl]-4-[(pyrrolidin-1-yl)methyl]oxazole (II). II exhibited affinity for the H3 receptor with Ki of 1.6 nM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1265299 HCAPLUS
DOCUMENT NUMBER: 144:22939
TITLE: Preparation of bicyclic heterocycles, particularly pyrimido[2,1-c][1,4]oxazine-2-carboxamides, as HIV integrase inhibitors
INVENTOR(S): Naidu, B. Narasimhulu; Banville, Jacques; Beaulieu, Francis; Connolly, Timothy P.; Krystal, Mark R.; Matiskella, John D.; Ouellet, Carl; Plamondon, Serge; Remillard, Roger; Sorenson, Margaret E.; Ueda, Yasutsugu; Walker, Michael A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 156 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005267105	A1	20051201	US 2005-126891	20050511
US 7176196	B2	20070213		
AU 2005250356	A1	20051215	AU 2005-250356	20050512
CA 2568356	A1	20051215	CA 2005-2568356	20050512
WO 2005118593	A1	20051215	WO 2005-US16473	20050512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1749011	A1	20070207	EP 2005-750075	20050512
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV, MK, YU				
US 2005267132	A1	20051201	US 2005-138726	20050526
US 2005267131	A1	20051201	US 2005-138773	20050526
US 7173022	B2	20070206		
WO 2005118589	A1	20051215	WO 2005-US18567	20050527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,				

NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

WO 2005118590 A1 20051215 WO 2005-US18568 20050527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

EP 1749008 A1 20070207 EP 2005-758639 20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV,
MK, YU

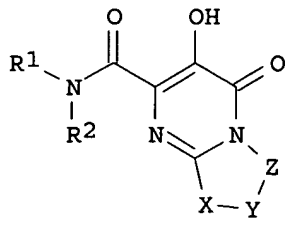
EP 1753767 A1 20070221 EP 2005-754152 20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV,
MK, YU

US 2006199956 A1 20060907 US 2005-288533 20051129
US 7157447 B2 20070102
US 2006276466 A1 20061207 US 2006-505149 20060816

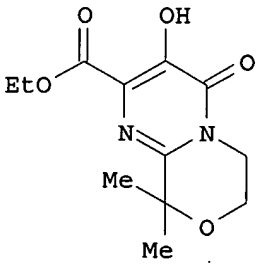
PRIORITY APPLN. INFO.:

US 2004-575513P	P	20040528
US 2004-603371P	P	20040820
US 2005-126891	A	20050511
WO 2005-US16473	W	20050512
US 2005-138726	A	20050526
US 2005-138773	A	20050526
WO 2005-US18567	W	20050527
WO 2005-US18568	W	20050527

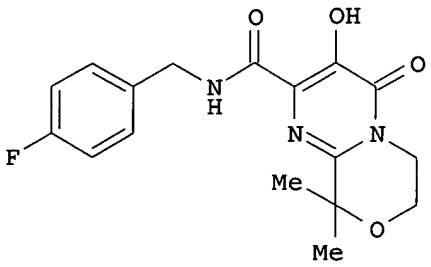
OTHER SOURCE(S): MARPAT 144:22939
GI



I



II



II

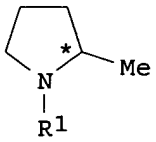
AB The invention is related to the preparation of title compds. I [R1 = C1-6(Ar1)alkyl, C1-6(Ar1)oxyalkyl, C1-6(Ar1)hydroxyalkyl, etc.; R2 = H, alkyl, OH, alkyloxy; Ar1 = (un)substituted Ph, naphthyl, benzothiophenyl, etc.; X-Y-Z = C(R3)2OC(R3)2, C(R3)2OC(R3)2C(R3)2, C(R3)2C(R3)2C(R3)2C(R3)2; R3 = H, alkyl], and their pharmaceutically acceptable salts or solvates which inhibit HIV integrase and prevent viral integration into human DNA. The invention is also related to the pharmaceutical compns. comprising pyrimidinones I, and methods of using them for treating HIV infection and AIDS. Thus, reacting ester II (preparation given) with 4-fluorobenzylamine in DMF/ethanol in the presence of TEA at 90° gave amide III in 82% yield. Selected I displayed IC50 values in the range of 0.002-0.1 μM for the inhibition of HIV integrase activity. II demonstrated synergistic or additive-synergistic HIV antiviral activity when used in combination with other antiviral agents, e.g., zidovudine, indinavir, T-20, etc.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

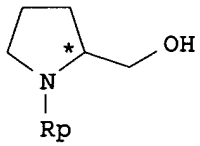
L15 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127154 HCAPLUS
DOCUMENT NUMBER: 142:74442
TITLE: Process for preparing 2-methylpyrrolidine and specific enantiomers thereof
INVENTOR(S): Ku, Yi-Yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004260100	A1	20041223	US 2004-789106		20040227
PRIORITY APPLN. INFO.:			US 2003-450480P	P	20030227

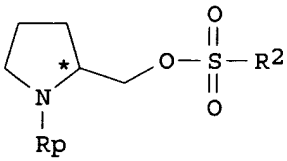
OTHER SOURCE(S): MARPAT 142:74442
GI



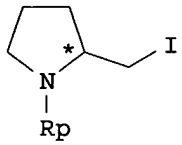
I



II



III



IV

AB The invention relates to a process for preparing 2-methylpyrrolidine or N-protected 2-methylpyrrolidine (I) (R1 = H, a nitrogen-protecting group; * denotes an asym. carbon atom) and, more particularly, specific enantiomers of I. The compound I is useful as an intermediate to obtain a compound useful for modulating a histamine-3 receptor. Novel intermediates also such as N-protected prolinol (II) (Rp = a nitrogen-protecting group) and their sulfonate ester (III) [Rp = same as above; R2 = each (un)substituted alkyl or aryl], and 2-iodomethylpyrrolidine (IV) (Rp = same as above) are described. Thus, N-protection of (S)-prolinol by di-tert-Bu dicarbonate followed by esterification with methanesulfonyl chloride gave (S)-2-[(methanesulfonyloxy)methyl]pyrrolidine-1-carboxylic acid tert-Bu ester which was iodinated by NaI to give (S)-2-iodomethylpyrrolidine-1-carboxylic acid tert-Bu ester (V). Hydrogenolysis of V over 10% Pd-C gave (R)-2-methylpyrrolidine-1-carboxylic acid tert-Bu ester which was treated with HCl in EtOAc to give (R)-2-methylpyrrolidine hydrochloride.

L15 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:722955 HCAPLUS
DOCUMENT NUMBER: 141:243334
TITLE: An efficient and cost-effective process for preparing 2-methylpyrrolidine and specific enantiomers thereof from (R/S)-prolinol
INVENTOR(S): Ku, Yi-yin; Cowart, Marlon D.; Sharma, Padam N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171845	A1	20040902	US 2003-376534	20030227
CA 2515801	A1	20040910	CA 2004-2515801	20040225
WO 2004076388	A2	20040910	WO 2004-US5573	20040225
WO 2004076388	A3	20041202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1601650	A2	20051207	EP 2004-714598	20040225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006519233	T	20060824	JP 2006-503863	20040225
PRIORITY APPLN. INFO.:			US 2003-376534 A	20030227
			WO 2004-US5573 W	20040225

OTHER SOURCE(S): MARPAT 141:243334

AB The invention relates to an efficient and cost-effective process for preparing 2-methylpyrrolidine and, more particularly, specific enantiomers of 2-methylpyrrolidine, from (R/S)-prolinol. Novel intermediates also are described. The title compds. were synthesized in several steps via N-protection of corresponding chiral prolinols, conversion of the hydroxy groups to sulfonates or iodides, reduction and finally N-deprotection. The iodides could also be prepared from the corresponding sulfonates via reaction with metal iodides. Thus, (S)-prolinol was N-protected with tert-butoxycarbonyl anhydride (100% yield) followed by sulfonylation with mesyl chloride (96% yield). The resulting mesylate was either directly reduced to (R)-N-Boc-2-methylpyrrolidine with lithium triethoxyborohydride (54% yield) or via the iodide intermediate through iodination with LiI (79% yield) followed by hydrogenolysis in the presence of Pd/C (85.9% yield). (R)-N-Boc-2-methylpyrrolidine was then deprotected with HCl to give 2-(R)-methylpyrrolidine hydrochloride (96% yield).

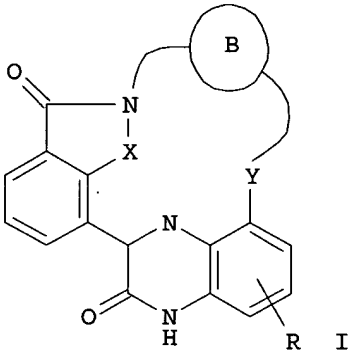
L15 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:390252 HCAPLUS
DOCUMENT NUMBER:	140:406823
TITLE:	Preparation of quinoxaline derivatives as Cdk inhibitors
INVENTOR(S):	Hirai, Hiroshi; Kawanishi, Nobuhiko; Hirose, Masaaki; Sugimoto, Tetsuya; Kamijyo, Kaori; Shibata, Jun; Masutani, Kouta
PATENT ASSIGNEE(S):	Banyu Pharmaceutical Co., Ltd., Japan
SOURCE:	PCT Int. Appl., 306 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039809	A1	20040513	WO 2003-JP13707	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503663	A1	20040513	CA 2003-2503663	20031027
AU 2003275681	A1	20040525	AU 2003-275681	20031027

EP 1557418	A1	20050727	EP 2003-758937	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006019959	A1	20060126	US 2005-532677	20050615
PRIORITY APPLN. INFO.:			JP 2002-313588 A	20021029
			WO 2003-JP13707 W	20031027

OTHER SOURCE(S): MARPAT 140:406823
GI



I

AB The title compds. I [X is NH, S, or the like; Y is O or the like; ring B is -B1(B1')B2(B2')B3(B3')B4(B4')B5(B5')-, etc.; B1 - B5 are each independently CH, N, or the like; and B1' - B5' are each independently hydrogen or the like; and R is hydrogen, lower alkyl, or the like] are prepared Compds. of this invention in vitro showed IC50 values of 1.6 nM to 34 nM against cyclin D2-cdk4.

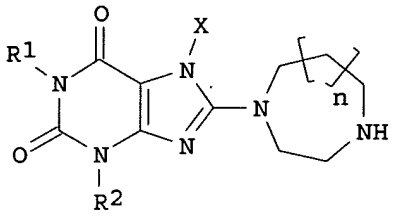
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:675555 HCAPLUS
DOCUMENT NUMBER: 139:197299
TITLE: Preparation of xanthine derivatives as DPP-IV inhibitors
INVENTOR(S): Yoshikawa, Seiji; Emori, Eita; Matsuura, Fumiyoshi; Clark, Richard; Ikuta, Hironori; Yasuda, Nobuyuki; Nagakura, Tadashi; Yamazaki, Kazuto; Aoki, Mika
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 217 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

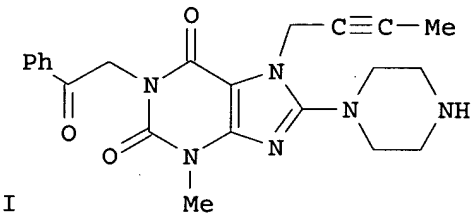
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1338595	A2	20030827	EP 2003-290431	20030224
EP 1338595	A3	20031008		
EP 1338595	B1	20060503		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

JP 2004043429	A	20040212	JP 2003-44771	20030221
US 2004082570	A1	20040429	US 2003-374918	20030224
US 7074798	B2	20060711		
PRIORITY APPLN. INFO.:			JP 2002-47761	A 20020225
			JP 2002-149557	A 20020523

OTHER SOURCE(S): MARPAT 139:197299
GI



I



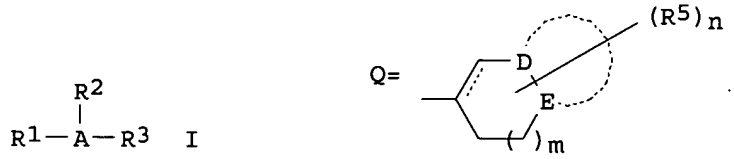
II

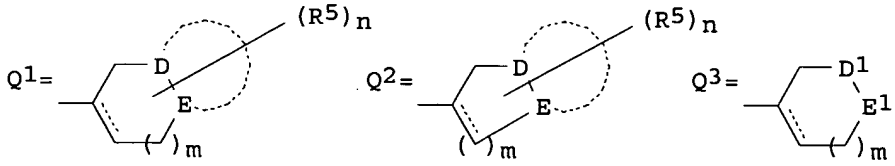
AB Novel xanthine derivs. of formula I [R1, R2 = H, alkyl, alkoxy, hydroxyalkyl, cycloalkyl, aryl, etc.; X = alkynyl, (substituted) Ph; n = 0, 1] are prepared which exhibit an excellent dipeptidyl peptidase IV (DPPIV) inhibition effect. Thus, II was prepared, and inhibited DPPIV with IC50 of 0.654 nM, and improved glucose tolerance in mice by 49.4%.

L15 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:905860 HCAPLUS
DOCUMENT NUMBER: 138:4600
TITLE: Preparation of heterocyclic compounds and pharmaceutical composition containing them for prevention or treatment of arthritis
INVENTOR(S): Ushiyama, Shigeru; Kimura, Tomio
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 501 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094267	A1	20021128	WO 2002-JP5018	20020523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003040776	A	20030213	JP 2002-149039	20020523
PRIORITY APPLN. INFO.:			JP 2001-155032	A 20010524

OTHER SOURCE(S): MARPAT 138:4600
GI





AB The invention relates to a pharmaceutical composition for prevention or treatment of arthritis such as chronic articular rheumatism and osteoarthritis which is useful in administering both a disease modifying antirheumatic drug (DMARD) and a compound represented by the general formula (I) or a pharmacol. acceptable salt, ester or other derivative thereof simultaneously, sep., or at a time interval [wherein A is a trivalent group derived from optionally substituted benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, or isothiazole; R1 is an optionally substituted aryl or heteroaryl; R2 is optionally substituted heteroaryl; and R3 is a group having the general formula Q-Q3 [wherein the bond accompanied by a dotted line represents a single or double bond; m is 1 or 2; R5 is hydrogen, HO, NO2, cyano, halo, lower alkoxy, lower haloalkoxy, lower alkylthio, etc.; n is 1 to 3; either D or E is nitrogen and the other is optionally substituted CH; one of D1 and E1 is optionally substituted NH and the other is optionally substitute CH2; and ring B containing D and E is a 4- to 7-membered heterocycle; provided that the constituent atoms of ring A to which R1 and R2 are bonded are each adjacent to the constituent atom of ring A to which R2 is bonded]]. Thus, 4.36 mL 1.6 M BuLi/hexane was added to a solution of 3.00 g 4-bromo-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1-triisopropylsilyl-1H-pyrrole in 60 mL THF at -78° and stirred for 10 min, followed by adding 1.29 g (2R,8aS)-2-methoxy-1,2,3,5,6,7,8,8a-octahydroindolidin-7-one at -78°, and the resulting mixture stirred at -78° and at room temperature for 1 h to give, after workup and desilylation with Bu4NF in THF, 22% 2-(4-fluorophenyl)-4-[(2R,8aS)-2-methoxy-1,2,3,5,8,8a-hexahydroindolizin-7-yl]-3-(pyridin-4-yl)-1H-pyrrole (II). Pharmaceutical formulations, e.g. a powder containing II, were described. 2-(4-Fluorophenyl)-4-[(8aS)-1,2,3,5,8,8a-hexahydroindolizin-7-yl]-3-(pyridin-4-yl)-1H-pyrrole at 2 mg/kg p.o. and leflunomide at 1 mg/kg p.o. daily for 17 days inhibited the dead Mycobacterium butyricum (adjuvant)-induced arthritis in Lewis rats by 52.3% compared to 12.6 and 13.9% when II (R = H) at 2 mg/kg and leflunomide at 1 mg/kg were administered alone, resp.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:888746 HCAPLUS
DOCUMENT NUMBER: 138:4599

TITLE: Preparation of fused imidazolidine derivatives as inhibitors of cartilage matrix degradation

INVENTOR(S): Funabashi, Yasunori; Takizawa, Masayuki; Morimoto, Shinji; Notoya, Kohei

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 940 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

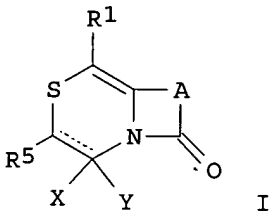
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092606	A1	20021121	WO 2002-JP4640	20020514
WO 2002092606	A8	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003034691	A	20030207	JP 2002-139642	20020515

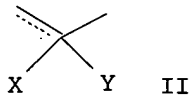
PRIORITY APPLN. INFO.: JP 2001-144608 A 20010515

OTHER SOURCE(S): MARPAT 138:4599

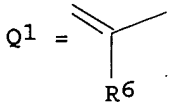
GI

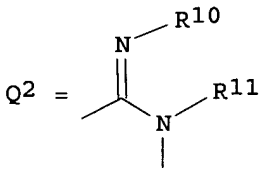


I



II





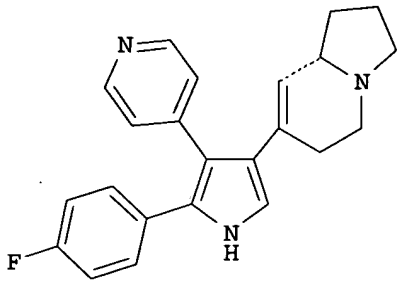
AB The title compds. I [R1 = (S)nR2, etc.; n = 0 - 2; R2 = H, (un)substituted hydrocarbon, etc.; R5 = H, (un)substituted hydrocarbon, etc.; the moiety represented by II in I is Q1, etc.; R6 = H, (un)substituted hydrocarbon, etc.; A = Q2, etc.; R10 = H, ZR15, etc.; Z = SO2, etc.; R15 = (un)substituted hydrocarbon, etc.; R11 = H, (un)substituted hydrocarbon] are prepared A process for preparing I is disclosed. Compds. of this invention in vitro at 0.1 μM gave 20% to 55% inhibition of MMP-13 production Formulations are given.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

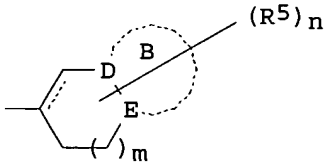
L15 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:793467 HCAPLUS
DOCUMENT NUMBER: 137:310916
TITLE: Preparation of (hexahydroindolidinyl)pyrrole, -thiophene, -pyrazole, and -imidazole derivatives as cytokine production inhibitors and their novel medicinal use in combination with nonsteroidal antiinflammatory agents
INVENTOR(S): Ushiyama, Shigeru; Kimura, Tomio
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 521 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

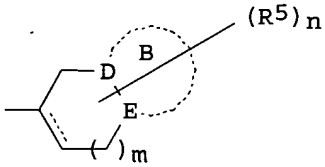
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080974	A1	20021017	WO 2002-JP3354	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2002363104	A	20021218	JP 2002-101720	20020403

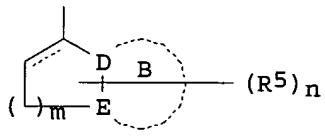
PRIORITY APPLN. INFO.: JP 2001-105615 A 20010404
OTHER SOURCE(S): MARPAT 137:310916
GI

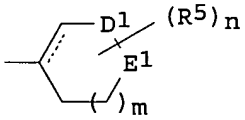


II

Q= 

Q1= 

Q2= 

Q3= 

AB Disclosed is a drug having relieved side effects of a nonsteroidal antiinflammatory agent (NSAID) which is to be used for simultaneously, sep., or intermittently during administering the nonsteroidal antiinflammatory agent, in particular having cyclooxygenase inhibitory activity, with an inflammatory cytokine production inhibitor. The active ingredient of the inflammatory cytokine production inhibitor is a compound represented by the general formula R1R2A-R3 [I; wherein A = an (un)substituted trivalent group selected from benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, and isothiazole; R1 = each (un)substituted aryl or heteroaryl; R2 = (un)substituted heteroaryl containing at least one N atom; R3 = Q-Q3; wherein m = 1,2; n = 1-3; R5 = H, HO, NO2, cyano, halo, lower alkoxy, halo-lower alkoxy, lower alkylthio, lower alkyl, lower alkenyl, lower alkynyl, aralkyl, oxo, hydroxyimino, lower alkoxyimino, lower alkylene, etc.; one of D and E is N and the other one is (un)substituted CH; one of D1 and E1 is (un)substituted NH and the other one is (un)substituted CH2; the ring B containing D and E = a 4- to 7-membered heterocyclic ring optionally fused with aryl, heteroaryl, cycloalkyl, or heterocyclyl group; a proviso is given]. The above compound alleviates the side effects, in particular stomach mucus membrane injury such as erosion or ulcer, of NSAID having cyclooxygenase inhibitory activity such as Aspirin, Etodolac, Diclofenac sodium, Aceclofenac, Indometacin, Farnesol, Nabumetone, Ibuprofen, Ketoprofen, Loxoprofen sodium, Naproxen, Nimesulide, Oxaprozin, Zaltoprofen, Piroxicam, Lornoxicam, Meloxicam, Celecoxib, Rofecoxib, Valdecoxib, and Etoricoxib. The above drug is useful for prevention or treatment of inflammations, malignant tumors, Alzheimer's disease, chronic articular rheumatism, or arthritis. Thus, 1-(4-fluorophenyl)-3-(4-pyridyl)-4-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)pyrrole (II) at 30 mg/kg inhibited by 91% the injury of stomach mucous membrane induced by Diclofenac sodium (15 mg/kg) in rats. A powder, a granule, and a capsule

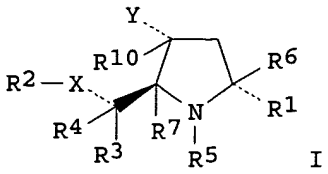
containing the specific compound I were described.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:730555 HCAPLUS
DOCUMENT NUMBER: 137:247920
TITLE: Preparation of pyrrolidine neuraminidase inhibitors
INVENTOR(S): Maring, Clarence J.; Gu, Yu Gui; Chen, Hui-Ju; Chen, Yuanwei; Degoey, David A.; Flosi, William J.; Giranda, Vincent L.; Grampovnik, David J.; Kati, Warren M.; Kempf, Dale J.; Kennedy, April; Klein, Larry L.; Krueger, Allan C.; Lin, Zhen; Madigan, Darold L.; McDaniel, Keith F.; Muchmore, Steven W.; Sham, Hing L.; Stewart, Kent D.; Stoll, Vincent S.; Sun, Minghua; Tu, Noah P.; Wagenaar, Frank L.; Wang, Gary T.; Wang, Sheldon; Wiedeman, Paul E.; Xu, Yibo; Yeung, Ming C.; Zhao, Chen; Hanessian, Stephen; Bayrakdarian, Malken; Luo, Xuehong
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 253 pp., Cont.-in-part of U.S. Ser. No. 282,139, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

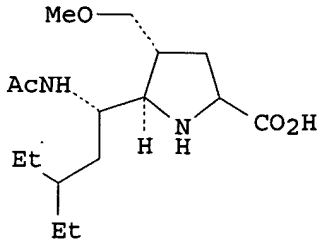
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6455571	B1	20020924	US 1999-421787	19991019
CA 2388859	A1	20010426	CA 2000-2388859	20001010
WO 2001028996	A2	20010426	WO 2000-US27910	20001010
WO 2001028996	A3	20011129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2003513889	T	20030415	JP 2001-531796	20001010
BR 2000010555	A	20030923	BR 2000-10555	20001010
EP 1358154	A2	20031105	EP 2000-972042	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2004097471	A1	20040520	US 2002-253152	20020924
US 6831096	B2	20041214		

PRIORITY APPLN. INFO.:		
US 1998-82828P	P	19980423
US 1999-282139	B2	19990331
US 1999-421787	A	19991019
WO 2000-US27910	W	20001010

OTHER SOURCE(S): MARPAT 137:247920
GI



I



II

AB Pyrrolidines I [X = (un)substituted CONH, NHCO, CSNH, NHCS, NHSO2, SO2NH; Y = H, (halo)alkyl, (halo)alkenyl, alkynyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), cycloalkenylalkenyl, (halo)phenyl, etc.; R1 = (CH2)CO2H, (CH2)SO3H, (CH2)SO2H, (CH2)PO3H2, (CH2)PO2H, tetrazolyl(methyl), etc.; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, haloalkyl, or haloalkenyl; or R2X = (un)substituted heterocyclyl; R3, R4 = H, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, acyl, etc.; or R3R4C = carbocyclyl or heterocyclyl; R5 = H, alkynyl, cyclopropyl cyclobutyl, or (un)substituted Me, OH, acyl, imino, NH2, etc.; R6, R7 = H, alkyl, alkenyl cycloalkyl(alkyl), cycloalkylalkenyl, cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl)arylalkenyl, heterocyclyl(alkyl), heterocyclylalkenyl; R10 = H, (cyclo)alkyl, (cyclo)alkenyl, fluoro], having relative or absolute configuration, were prepared as neuraminidase inhibitors for the treatment of diseases caused by microorganisms having a neuraminidase, especially influenza neuraminidase. For example, (±)-II•HCl was synthesized in an 11-step sequence involving (1) cycloaddn. of acrolein and t-Bu N-benzylglycinate to give (±)-(2S,3RS,5R)-1-benzyl-2-vinyl-3-formylpyrrolidine-5-carboxylic acid t-Bu ester (45%), (2) reduction of the aldehyde to the alc. (66%), (3) O-protection using t-butyldimethylsilyl chloride (71%), (4) oxidation of the vinyl group to an aldehyde (46%), (5) addition of 1-bromo-2-ethylbutane to the aldehyde (66%), (6) reductive amination of the ketone (64%), (7) amidation with AcOAc (72%), (8) deprotection of the alc. (61%), (9) etherification of the alc. with iodomethane, (10) N-deprotection (47%), and (11) deesterification and salt formation using 6N HCl. I inhibit influenza A and influenza B neuraminidase with Ki values for preferred compds. in the range 0.1 nM to 3.5 μM. In a cell culture plaque formation inhibition assay, I inhibited influenza virus A/N2/Tokyo in MDCK cells with EC50 values between 100 μM and 1 nM; preferred compds. gave EC50 values between 1 μM and 1 nM.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

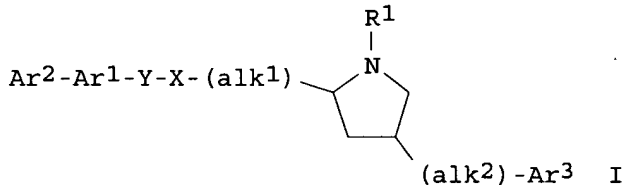
L15 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:487555 HCAPLUS
DOCUMENT NUMBER: 137:47220
TITLE: Preparation of substituted pyrrolidines as CCR-3 receptor antagonists
INVENTOR(S): Kertesz, Denis John; Roepel, Michael Garret
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

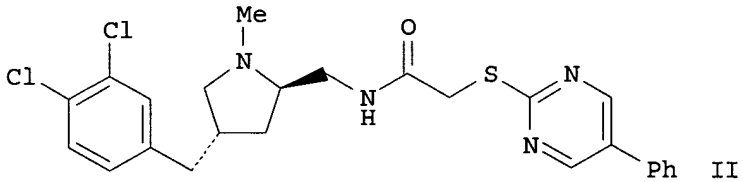
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002050064	A1	20020627	WO 2001-EP14670		20011213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2431767	A1	20020627	CA 2001-2431767		20011213
AU 2002016107	A5	20020701	AU 2002-16107		20011213
EP 1358181	A1	20031105	EP 2001-271370		20011213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001016352	A	20031202	BR 2001-16352		20011213
JP 2004519443	T	20040702	JP 2002-551560		20011213
US 2002198255	A1	20021226	US 2001-34034		20011219
US 6552028	B2	20030422			
US 2003199532	A1	20031023	US 2003-368097		20030218
ZA 2003004530	A	20040910	ZA 2003-4530		20030610
PRIORITY APPLN. INFO.:			US 2000-256585P	P	20001219
			WO 2001-EP14670	W	20011213
			US 2001-34034	A3	20011219

OTHER SOURCE(S): MARPAT 137:47220

GI



I



II

AB The title compds. [I; R1 = H, C1-6 alkyl, acyl, heteroalkyl, -CONR3R4 (where R3, R4 = H, C1-6 alkyl), -CO2R5 (where R5 = H, C1-6 alkyl, heteroalkyl), SO2R6 (where R6 = C1-6 alkyl); alk1 = C1-6 alkylene; X = NHCO, CONH; Y = C1-3 alkylene, C2-3 alkylene wherein one of the carbon atoms is replaced by a heteroatom selected from the group consisting of O, NRb [where Rb = H, C1-6 alkyl, acyl, CONR7R8 (where R7, R8 = H, C1-6 alkyl), CO2R9 (where R9 = H, C1-6 alkyl, heteroalkyl), aryl, aryl C1-6 alkyl] and S(O)n (wherein n is an integer from 0 to 2); Ar1 = a heteroaryl group or Ph wherein the heteroaryl or Ph group is substituted, in addition to the Ar2 group, with a group selected from the group consisting of H, halo, C1-6 alkyl, C1-6 alkoxy, NO2, amido, aminosulfonyl and sulfonylamino; Ar2 = aryl; alk2 = C1-6 alkylene wherein one of the carbon atoms is optionally replaced by CO, NRc [where Rc = H, C1-6 alkyl, acyl, -CONR10R11 (where

R11, R12 = H, C1-6 alkyl), CO2R12 (where R12 = H, C1-6 alkyl, heteroalkyl), aryl, aryl C1-6 alkyl] or S(O)n1 (wherein n1 is an integer from 0 to 2); Ar3 = C3-7 cycloalkyl, aryl, heteroaryl] or pharmaceutically acceptable salts thereof are prepared The compds. are useful as CCR-3 receptor antagonists and, therefore, may be used for the treatment of diseases treatable by administration of a CCR-3 receptor antagonists, e.g. asthma. Thus, to a solution of (2R,4S)-2-aminomethyl-3-(3,4-dichlorobenzyl)-1-methylpyrrolidine (24 mg, 0.088 mmol) in CH2Cl2 (5 mL) was added 5-phenylpyrimidin-2-ylthioacetic acid (24 mg, 0.097 mmol), EDCl (21 mg, 0.11 mmol) and HOBT (1 mg, 0.009 mmol) and the reaction mixture was stirred for 2 h at room temperature to give, after workup, N-[2-[(2R,4S)-4-(3,4-dichlorobenzyl)-1-methylpyrrolidin-2-yl]methyl]-2-[(5-phenylpyrimidin-2-yl)thio]acetamide (II). II showed IC50 of 0.028 μM for inhibiting the binding of [125I]eotaxin to CCR-3 L1.2 transfectant cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

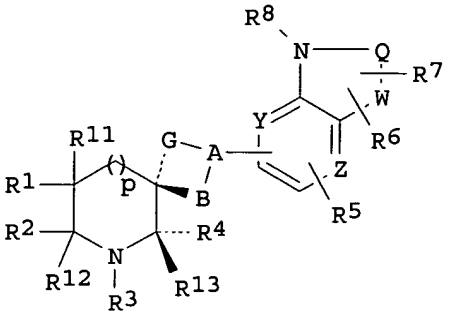
L15 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:762988 HCAPLUS
DOCUMENT NUMBER: 135:331346
TITLE: Synthesis of benzoamide piperidine containing compounds as substance P antagonists
INVENTOR(S): Arnold, Eric Platt; Chappie, Thomas Allen; Huang, Jianhua; Humphrey, John Michael; Nagel, Arthur Adam; O'Neill, Brian Thomas; Sobolov-Jaynes, Susan Beth; Vincent, Lawrence Albert
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 209 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077100	A2	20011018	WO 2001-IB629	20010406
WO 2001077100	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003087925	A1	20030508	US 2001-811218	20010316
US 7119207	B2	20061010		
CA 2405089	A1	20011018	CA 2001-2405089	20010406
EP 1272484	A2	20030108	EP 2001-919702	20010406
EP 1272484	B1	20050720		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009936	A	20030506	BR 2001-9936	20010406
HU 200300413	A2	20030628	HU 2003-413	20010406
JP 2004501072	T	20040115	JP 2001-575573	20010406
EE 200200588	A	20040415	EE 2002-588	20010406
NZ 521346	A	20040730	NZ 2001-521346	20010406
AT 299875	T	20050815	AT 2001-919702	20010406

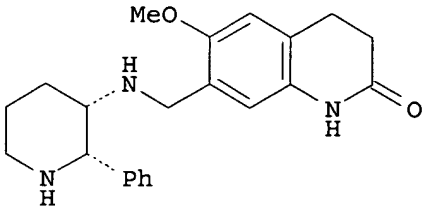
ES 2244599	T3	20051216	ES 2001-1919702		20010406
IN 2002MN01244	A	20050304	IN 2002-MN1244		20020912
BG 107135	A	20030630	BG 2002-107135		20020923
ZA 2002008072	A	20031008	ZA 2002-8072		20021008
NO 2002004874	A	20021118	NO 2002-4874		20021009
PRIORITY APPLN. INFO.:			US 2000-195922P	P	20000410
			US 2000-212922P	P	20000620
			WO 2001-IB629	W	20010406

OTHER SOURCE(S): MARPAT 135:331346

GI



I



II

AB Title compds. I [Q = C:NH, C:CH2, C:S, C:O, SO, SO2; A = CH, CH2, C(alkyl), CH(alkyl), C(CF3), or CH(CF3) with the proviso that when B is present, A = CH, C(alkyl), or C(CF3); B = absent, CH2, or ethylene; Y, Z = N, CH, provided that both are not N; G = NH(CH2)q, S(CH2)q, O(CH2)q; q = 0-1 with the proviso that when q = 0, G = NH2, SH, OH; W = 1-3 carbon linking group, including spiro assemblies; p = 0-2; R3 = H, acyl, carboxy, Ph, heterocyclyl, alkyl, etc.; R1, R2, R11-13 = H, alkyl, etc., or R12-13 together with the carbon atoms to which they are attached form a 5- or 6-membered heterocyclic ring, etc.; R4 = Ph, pyridyl, thienyl, etc.; R5-8 = H, alkyl, S(O)1-2-alkyl, S(O)1-2-aryl, alkoxy, halo, Ph, etc.] were prepared Approx. 100 synthetic examples and over 100 precursor prepns. were provided. For instance, 4-aminophenol was acylated with 3-chloropropionyl chloride (CH2Cl2, H2O, NaHCO3, room temperature, 4 h) and the product treated with AlCl3 at 210°C for 10 min effecting cyclization to the hydroxy quinolone intermediate. The intermediate was O-methylated (acetone, Me2SO4, K2CO3, room temperature, 16 h) and formylated in the 7 position (CH2Cl2, AlCl3, Cl2CHOMe) to give 7-formyl-6-methoxy-1H-1,2,3,4-tetrahydroquinolin-2-one. Reductive alkylation of the quinolone with (2S,3S)-3-amino-2-phenylpiperidine (a. PhMe, 3Å mol. sieves; b. dichloroethane, NaHB(OAc)3, room temperature, 16 h) yielded II. Compds. I are NK-1 receptor

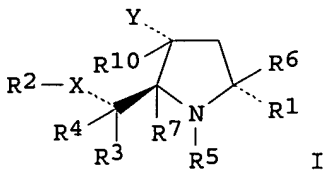
antagonists, i.e., substance P receptor antagonists. At least one stereoisomer of the example compds. had a binding affinity, as measured by Ki, of at least 600 nM. I are used in the treatment and prevention of a wide variety of central nervous system disorders, inflammatory disorders, cardiovascular disorders, ophthalmic disorders, etc.

L15 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:300677 HCAPLUS
DOCUMENT NUMBER: 134:326397
TITLE: Preparation of pyrrolidine neuraminidase inhibitors
INVENTOR(S): Maring, Clarence J.; Giranda, Vincent L.; Kempf, Dale J.; Stoll, Vincent S.; Sun, Minghua; Zhao, Chen; Gu, Yu Gui; Hanessian, Stephen; Wang, Gary T.; Krueger, Allan C.; Chen, Hui-ju; Chen, Yuanwei; Degoey, David A.; Flosi, William J.; Grampovnik, David J.; Kati, Warren M.; Kennedy, April L.; Klein, Larry L.; Lin, Zhen; Madigan, Darold L.; Mcdaniel, Keith F.; Muchmore, Steven W.; Sham, Hing L.; Stewart, Kent D.; Tu, Noah P.; Wagenaar, Frank L.; Wang, Sheldon; Wiedeman, Paul E.; Xu, Yibo; Yeung, Ming C.; Bayrakdarian, Malken; Luo, Xuehong
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 714 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

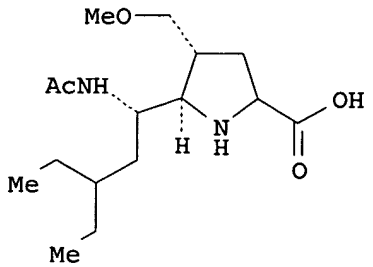
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028996	A2	20010426	WO 2000-US27910	20001010
WO 2001028996	A3	20011129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6455571	B1	20020924	US 1999-421787	19991019
CA 2388859	A1	20010426	CA 2000-2388859	20001010
JP 2003513889	T	20030415	JP 2001-531796	20001010
BR 2000010555	A	20030923	BR 2000-10555	20001010
EP 1358154	A2	20031105	EP 2000-972042	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:		
US 1999-421787	A	19991019
US 1998-82828P	P	19980423
US 1999-282139	B2	19990331
WO 2000-US27910	W	20001010

OTHER SOURCE(S): MARPAT 134:326397
GI



I



II

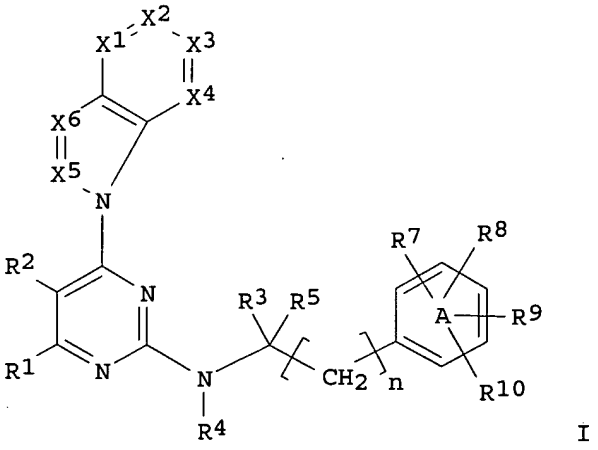
AB Title compds. (I) [wherein X = (un)substituted CONH, NH, CSNH, NHCS, NHSO2, SO2NH; Y = H, (halo)alkyl, (halo)alkenyl, alkynyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), cycloalkenylalkenyl, (halo)phenyl, N(O):CHCH3, halo, heterocyclyl, or (un)substituted (CH2)nOH, CH(OH)CH2(OH), (CH2)nSH, (CH2)nCN, (CH2)nN3, (CH2)nNH2, etc.; n = 0-2; R1 = (CH2)CO2H, (CH2)SO3H, (CH2)SO2H, (CH2)PO3H2, (CH2)PO2H, tetrazolyl(methyl), (CH2)CONHSO2R11, or (un)substituted (CH2)SO2NH2; R11 = alkyl, alkenyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl), arylalkenyl, heterocyclyl(alkyl), or heterocyclylalkenyl; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, haloalkyl, or haloalkenyl; or R2X = (un)substituted heterocyclyl; R3 and R4 = independently H, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, or (un)substituted ketones, acids, amides, alc., thiols, etc.; or R3 and R4 taken together with the C to which they are attached form a carbocyclic or heterocyclic ring; R5 = H, alkynyl, cyclopropyl cyclobutyl, or (un)substituted Me, OH, acyl, imino, NH2, etc.; R6 and R7 = independently H, alkyl, alkenyl cycloalkyl(alkyl), cycloalkylalkenyl, cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl)arylalkenyl, heterocyclyl(alkyl), or heterocyclylalkenyl; R10 = H, (cyclo)alkyl, (cyclo)alkenyl, or fluoro] were prepared as neuraminidase inhibitors for the treatment of diseases caused by microorganisms having a neuraminidase, especially influenza neuraminidase. For example, (±)-II•HCl was synthesized in an 11-step sequence involving (1) cycloaddn. of acrolein and t-Bu N-benzylglycinate to give (±)-(2S,3RS,5R)-1-benzyl-2-vinyl-3-formylpyrrolidine-5-carboxylic acid t-Bu ester (45%), (2) reduction of the aldehyde to the alc. (66%), (3) O-protection using t-butyldimethylsilyl chloride (71%), (4) oxidation of the vinyl group to an aldehyde (46%), (5) addition of 1-bromo-2-ethylbutane to the aldehyde (66%), (6) reductive amination of the ketone (64%), (7) amidation with AcOAc (72%), (8) deprotection of the alc. (61%), (9) etherification of the alc. with iodomethane, (10) N-deprotection (47%), and (11) deesterification and salt formation using 6N HCl. I inhibit influenza A and influenza B neuraminidase with Ki values between 0.1 nM and 700 μM; Ki values for preferred compds. ranged from 0.1 nM to 3.5 μM. In a cell culture plaque formation inhibition assay, I inhibited influenza virus A/N2/Tokyo in MDCK cells with EC50 values between 100 μM and 1 nM; preferred compds. gave EC50 values between 1 μM and 1 nM.

L15 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:12273 HCAPLUS
DOCUMENT NUMBER: 134:86271
TITLE: Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds
INVENTOR(S): Armstrong, Helen M.; Beresis, Richard; Goulet, Joung L.; Holmes, Mark A.; Hong, Xingfang; Mills, Sander G.; Parsons, William H.; Sinclair, Peter J.; Steiner, Mark

G.; Wong, Frederick; Zaller, Dennis M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 470 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000213	A1	20010104	WO 2000-US17443	20000626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383546	A1	20010104	CA 2000-2383546	20000626
EP 1206265	A1	20020522	EP 2000-941701	20000626
EP 1206265	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6498165	B1	20021224	US 2000-604305	20000626
JP 2003523942	T	20030812	JP 2001-505922	20000626
AT 253915	T	20031115	AT 2000-941701	20000626
PRIORITY APPLN. INFO.:			US 1999-141639P P	19990630
			WO 2000-US17443 W	20000626

OTHER SOURCE(S): MARPAT 134:86271
GI



I

AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative

disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxycarbonyl, carbamoyl, acyloxy, alkoxycarbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example prepns. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

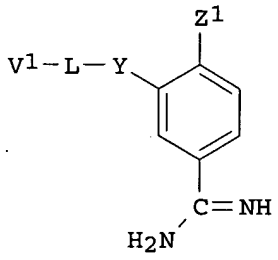
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795787 HCAPLUS
DOCUMENT NUMBER: 132:35700
TITLE: Preparation of benzamidine derivatives as activated blood coagulation factor X inhibitors
INVENTOR(S): Nakagawa, Tadakiyo; Sagi, Kazuyuki; Yoshida, Kaoru; Fukuda, Yumiko; Shoji, Masataka; Takehana, Shunji; Kayahara, Takashi; Takahara, Akira
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

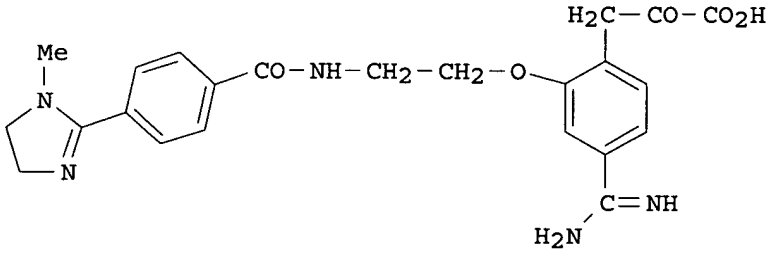
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964392	A1	19991216	WO 1999-JP3055	19990608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2334476	A1	19991216	CA 1999-2334476	19990608
AU 9940604	A	19991230	AU 1999-40604	19990608
AU 758567	B2	20030327		

EP 1086946	A1	20010328	EP 1999-923959	19990608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
US 2001056123	A1	20011227	US 2000-731729	20001208
US 6410538	B2	20020625		
US 2002107290	A1	20020808	US 2002-73985	20020214
US 6812231	B2	20041102		
PRIORITY APPLN. INFO.:			JP 1998-159627 A	19980608
			JP 1998-159628 A	19980608
			WO 1999-JP3055 W	19990608
			US 2000-731729 A1	20001208

OTHER SOURCE(S): MARPAT 132:35700
GI



I



II

AB The title compds. I [L is CH2CH2, etc.; Z1 is CH:CHCOR2, etc.; R2 is OH, etc.; Y is CH:CH, etc.; V1 is, for example, H, (un)substituted benzoyl, etc.; extensive details on V1 are given] are prepared I are useful as antithrombotics. In an in vitro test for inhibiting activity against activated blood coagulation factor X, the title compound II.2CF3CO2H showed pIC50 of 8.1.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

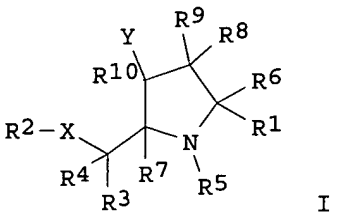
L15 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:691077 HCAPLUS
DOCUMENT NUMBER: 131:310834
TITLE: Preparation of pyrrolidines as inhibitors of neuraminidases
INVENTOR(S): Maring, Clarence J.; Gu, Yu-Gui; Chen, Hui-Ju; Chen, Yuanwei; Degoey, David A.; Flosi, William J.; Giranda, Vincent L.; Grampovnik, David J.; Kati, Warren M.; Kempf, Dale J.; Klein, Larry L.; Krueger, Allan C.; Lin, Zhen; Madigan, Darold L.; Mcdaniel, Keith F.; Muchmore, Steven W.; Sham, Hing L.; Stewart, Kent D.; Stoll, Vincent S.; Sun, Minghua; Wang, Gary T.; Wang,

Sheldon; Xu, Yibo; Yeung, Ming C.; Zhao, Chen; Kennedy, April
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 601 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954299	A1	19991028	WO 1999-US7945	19990412
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329422	A1	19991028	CA 1999-2329422	19990412
AU 9935545	A	19991108	AU 1999-35545	19990412
BR 9909870	A	20001219	BR 1999-9870	19990412
TR 200003065	T2	20010221	TR 2000-200003065	19990412
HU 200101224	A2	20010828	HU 2001-1224	19990412
JP 2002512224	T	20020423	JP 2000-544640	19990412
EP 1315698	A1	20030604	EP 1999-917414	19990412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
ZA 2000005238	A	20011204	ZA 2000-5238	20000928
NO 2000005301	A	20001208	NO 2000-5301	20001020
BG 104962	A	20010731	BG 2000-104962	20001117

PRIORITY APPLN. INFO.: US 1998-65225 A 19980423
WO 1999-US7945 W 19990412

OTHER SOURCE(S): MARPAT 131:310834
GI



I

AB Compds. I [R1 = CO2H, CH2CO2H, SO3H, CH2SO3H, SO2H, CH2SO2H, PO3H2, CH2PO3H2, PO2H, CH2PO2H, tetrazolyl, CH2-tetrazolyl, etc.; X = CONR, NRCO, C(S)NR, NRC(S), NRSO2, SO2NR, where R = H, alkyl, cyclopropyl; R2 = H, alkyl, alkenyl, cycloalkyl, etc. or R2X is 5-(un)substituted 2-oxopyrrolidinyl or 3-oxa, 3-thia, or 3-aza analogs; R3, R4 = H, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, (un)substituted aliphatic group; R5 = H, alkyl, OH, alkoxy, alkynyl, cyclopropyl, cyclobutyl, amino, etc.; Y = H, alkyl, haloalkyl, alkenyl, cycloalkyl, halophenyl, etc.; R6,

R7 = H, alkyl, alkenyl, cycloalkyl, aryl, etc.; R8, R9, R10 = H, alkyl, alkenyl, cycloalkyl, cycloalkenyl, F] were prepared as inhibitors of neuraminidases from disease-causing microorganisms, especially, influenza neuraminidase. Thus, (±)-(2S,3R,5R,1'S)-2-(1-acetamido-3-ethylpentyl)-3-(methoxymethyl)pyrrolidine-5-carboxylic acid hydrochloride was prepared by a multistep procedure starting with acrolein, tert-Bu N-benzylglycinate, and 1-bromo-2-ethylbutane.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

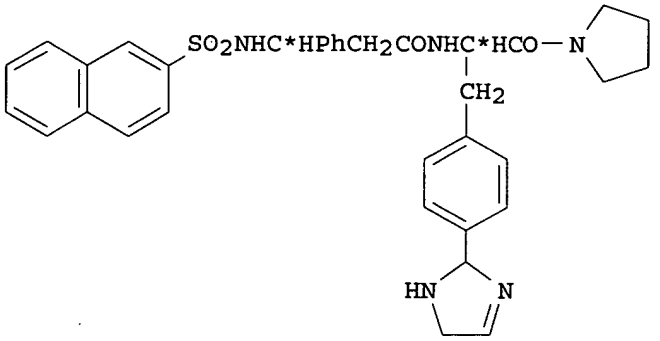
L15 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:564952 HCAPLUS
DOCUMENT NUMBER: 127:162118
TITLE: Novel N-(arylsulfonyl) amino acid derivatives having bradykinin receptor affinity
INVENTOR(S): Ferrari, Bernard; Gougat, Jean; Muneaux, Claude; Muneaux, Yvette; Perreaut, Pierre; Planchenault, Claudine
PATENT ASSIGNEE(S): Sanofi, Fr.; Ferrari, Bernard; Gougat, Jean; Muneaux, Claude; Muneaux, Yvette; Perreaut, Pierre; Planchenault, Claudine
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725315	A1	19970717	WO 1997-FR26	19970107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2743562	A1	19970718	FR 1996-269	19960111
FR 2743562	B1	19980403		
CA 2241788	A1	19970717	CA 1997-2241788	19970107
CA 2241788	C	20060912		
AU 9713832	A	19970801	AU 1997-13832	19970107
EP 877737	A1	19981118	EP 1997-900243	19970107
EP 877737	B1	20010801		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504315	T	20000411	JP 1997-524916	19970107
AT 203745	T	20010815	AT 1997-900243	19970107
ES 2162231	T3	20011216	ES 1997-900243	19970107
BR 9707120	A	19990720	BR 1997-7120	19971007
US 6015812	A	20000118	US 1998-101214	19980702
NO 9803190	A	19980710	NO 1998-3190	19980710
NO 310975	B1	20010924		
US 6100278	A	20000808	US 1999-434333	19991104
US 6313120	B1	20011106	US 2000-593067	20000613
US 6433185	B2	20020813	US 2001-948011	20010906
US 2002115685	A1	20020822		
US 2003073641	A1	20030417	US 2002-165299	20020607
US 6610882	B2	20030826		

PRIORITY APPLN. INFO.:

FR 1996-269	A	19960111
WO 1997-FR26	W	19970107
US 1998-101214	A3	19980702
US 1999-434333	A3	19991104
US 2000-593067	A3	20000613
US 2001-948011	A3	20010906

OTHER SOURCE(S): MARPAT 127:162118
GI



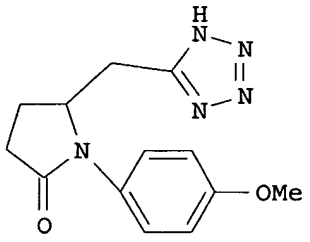
I

AB Arylsulfonyl amino acid derivs. RSO2NR1C*HR2CHR3CONR9C*R10[CH2C6H4C(:NR6)NR7R8-p]CONR4R5 [C* is an asym. carbon atom; R = (un)substituted Ph, naphthyl, tetrahydronaphthyl, quinolyl, or isoquinolyl; R1 = H, alkyl, (un)substituted phenylalkyl; R2 = (un)substituted Ph, phenylalkyl, naphthyl, cyclohexyl; R3 = H, OH; R4, R5 = H, alkyl or NR4R5 = (un)substituted heterocyclyl; R6, R8 = H, (un)substituted benzyl, alkyl, aminoalkyl, etc.; R7 = H, alkyl; R9, R10 = H, Me; or R1R9 = methylene] were prepared The compds. have bradykinin receptor affinity. Thus, arylsulfonyl amino acid (R,R)-I.HCl was prepared by amidation of (R)-3-(2-naphthylsulfonamido)-3-phenylpropionic acid hydroxysuccinimide ester with (R)-1-[2-amino-3-(4-cyanophenyl)propionyl]pyrrolidine trifluoroacetate, followed by reaction with ethylenediamine.

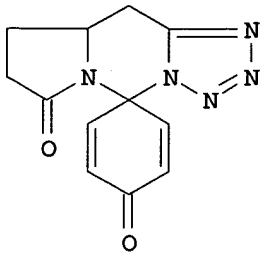
L15 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1996:457592 HCAPLUS
DOCUMENT NUMBER:	125:195238
TITLE:	Simple and condensed β-lactams. Part 27. Reaction of 1-(4-methoxyphenyl)-4-(tetrazol-5-yl)azetidin-2-one and 1-(4-methoxyphenyl)-5-(tetrazol-5-ylmethyl)pyrrolidin-2-one with cerium(IV) ammonium nitrate (CAN)
AUTHOR(S):	Giang, Le Thanh; Fetter, Jozsef; Lempert, Karoly; Kajtar-Peredy, Maria; Gomory, Agnes
CORPORATE SOURCE:	Dep. of Organic Chemistry, Technical Univ. Budapest, Budapest, H-1521, Hung.
SOURCE:	Tetrahedron (1996), 52(30), 10169-10184 CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 125:195238

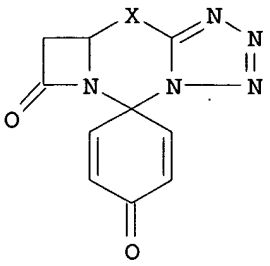
GI



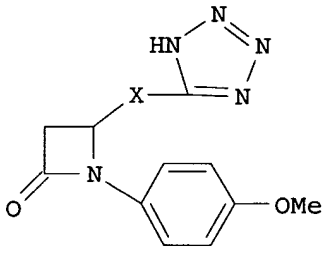
I



II



III



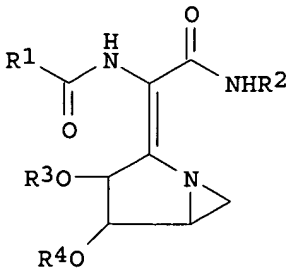
IV

AB Treatment of pyrrolidinone I with CAN under the usual conditions leads to formation of spiro compound II, rather than to N-demethoxyphenylation. A study of the reactions of compound II with sodium chloride and sodium iodide furnished the proof for the assumption that the related non-isolable compds. III (X = CH2, bond) are the intermediates of the anomalous reactions of compds. IV (X = CH2, bond) with CAN.

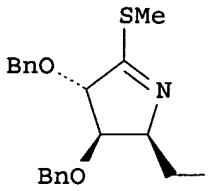
L15 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:271109 HCAPLUS
DOCUMENT NUMBER: 124:316977
TITLE: Preparation of 2-(1-acylamino-1-carbamoyl)methylene-1-aza-3,4-dihydroxybicyclo[3.1.0]hexane derivatives as anticancer agents
INVENTOR(S): Terajima, Atsuro; Hashimoto, Masaru; Yamada, Kaoru
PATENT ASSIGNEE(S): Sagami Chem Res, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08003133	A	19960109	JP 1994-140503	19940622
PRIORITY APPLN. INFO.:			JP 1994-140503	19940622

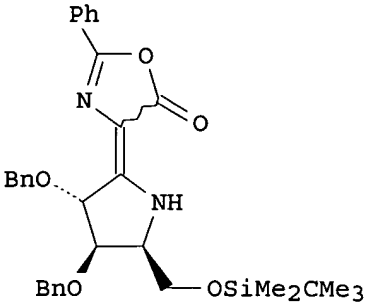
OTHER SOURCE(S): MARPAT 124:316977
GI



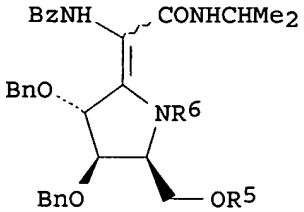
I



II



III



IV

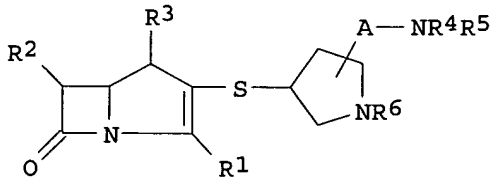
AB The title compds. [I; R1, R2 = C1-5 linear or branched alkyl, (un)substituted aralkyl or aryl; R3, R4 = (un)substituted aralkyl], which possess potent cytotoxicity, are prepared Thus, 5-methylthio-2H-pyrrole derivative (II) was condensed with 5-oxo-2-phenyl-Δ2-oxazoline in toluene for 5 h to give the (oxazolin-4-ylidene)pyrrolidine derivative (III), which was acylated by diallyl dicarbonate in the presence of 4-dimethylaminopyridine in THF at room temperature for 10 min and then underwent aminolysis with isopropylamine in THF at room temperature for 2 h to give (Z)- and (E)-2-(1-benzoylamino-2-N-isopropylcarbamoyl)methylenepyrrolidine derivative (IV; R5 = SiMe2CMe3, R6 = CO2CH2CH:CH2) in 20 and 45% yield, resp. This (E)- or (Z)-isomer was deprotected by treatment with Ph3P, [Ph3P]4Pd, and dimedone in THF and then with a mixture of concentrated HCl and HCl to give IV (R5 = R6 = H), which was mesylated by MeSO2Cl in CH2Cl2 containing Et3N to give the mesylate ester IV (R5 = SO2Me, R6 = H) in 65% yield. The latter compound in THF was treated with potassium hexamethyldisilazide in toluene and stirred at room temperature for 5 min tog vie the title compound I (R1 = Ph, R3 = R4 = PhCH2, R2 = CHMe2). This compound and I (R1 = Ph, R2 = R3 = R4 = PhCH2) showed IC50 of 3.1 and 12 μg/mL, resp., against mouse leukemia P388 cells.

L15 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:491987 HCAPLUS
DOCUMENT NUMBER: 122:239446
TITLE: Preparation of 3-pyrrolidinylthio-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid derivatives as antibacterial agents
PATENT ASSIGNEE(S): Fujisowa Pharmaceutical Co. Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 42 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

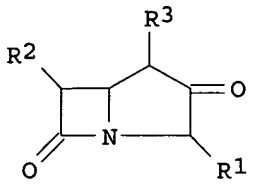
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06263761	A	19940920	JP 1994-6020	19940124
PRIORITY APPLN. INFO.:			GB 1993-1276 A	19930122

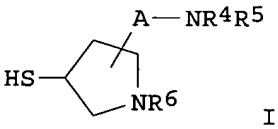
OTHER SOURCE(S): CASREACT 122:239446; MARPAT 122:239446
GI



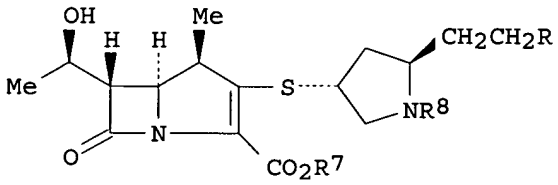
I



II



III



IV

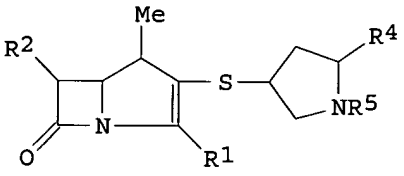
AB The title carbapenems [I; R1 = (un)protected CO2H; R2 = (un)protected hydroxyalkyl; R3 = H, lower alkyl; R4 = lower alkyl and R5 = lower alkyl or hydroxy-lower alkyl; or R4 = lower alkyl, lower alkenyl, HOCH2CH2, HO(CH2)3, 2-tri(lower alkyl)silylethyl, 3-tri(lower alkyl)silylpropyl, lower cyanoalkyl, lower halohydroxyalkyl, lower haloalkyl, carbamoyloxy-lower alkyl, H2NCOCH2, or H2NCOCHMe and R5 = H or imino-protecting group; R6 = H, imino-protecting group; A = lower alkylene, provided that when R4 = H2NCOCH2 or H2NCOCHMe, A = CH2CH2] are prepared by condensation of azabicyclo[3.2.0]heptanone derivative (II; R1 - R3 = same as above) with 3-mercaptopyrrolidine derivative (III; A, R4 - R6 = same as above). Thus, 80 mg rhodium(II) octanoate was added to a solution of 6.68 g allyl (4R)-2-diazo-4-[(2R,3S)-3-[(1R)-1-hydroxyethyl]-4-oxoazetidin-2-yl]-3-oxopentanoate in EtOAc, refluxed for 20 min, and evaporated under reduced pressure. The obtained residue was redissolved in MeCN followed by adding successively 4.9 mL di-Ph chlorophosphate, 4.4 mL (Me2CH)2NEt, and 14 mg 4-dimethylaminopyridine at 0° to give a solution of a phosphate ester. A thiol solution in N,N-dimethylacetamide, prepared via deprotection of (2R,4S)-1-allyloxycarbonyl-2-[2-(N,N-dimethylamino)ethyl]-4-triphenylmethylthiopyrrolidine with CF3CO2H and Et3Si in CH2Cl2 under ice-cooling, was added to the above phosphate ester solution at 0° followed by adding (Me2CH)2NEt (pH 8) and stirring the resulting mixture for 28 h at 0° to give carbapenem intermediate (IV; R = NMe2, R7 = allyl, R8 = allyloxycarbonyl). The latter compound was quaternized by alkylation with 2-iodoacetamide followed by deprotection with Ph3P, tetrakis(triphenylphosphine)palladium(0), and Bu3SnH in EtOH/THF to give title carbapenem IV (R = N+Me2CH2CONH2.Cl-, R7 = R8 = H), which showed

min. inhibitory concentration of 0.2 μg/mL for Pseudomonas aeruginosa.

L15 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:630576 HCAPLUS
DOCUMENT NUMBER: 121:230576
TITLE: Preparation of substituted 3-(pyrrolidinylthio)carbapenems as antimicrobial agents
INVENTOR(S): Murata, Masayoshi; Tsutsumi, Hideo; Matsuda, Keiji; Hattori, Kohji; Nakajima, Takashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321186	A1	19931028	WO 1993-JP469	19930409
W: AU, CA, HU, JP, KR, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9339044	A	19931118	AU 1993-39044	19930409
EP 636133	A1	19950201	EP 1993-908083	19930409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07505650	T	19950622	JP 1993-518180	19930409
JP 3367104	B2	20030114		
CN 1082547	A	19940223	CN 1993-105695	19930412
ZA 9302599	A	19931026	ZA 1993-2599	19930413
US 5608056	A	19970304	US 1994-302780	19940921
PRIORITY APPLN. INFO.:			GB 1992-8133 A	19920413
			GB 1992-20893 A	19921005
			GB 1993-3720 A	19930224
			WO 1993-JP469 A	19930409

OTHER SOURCE(S): MARPAT 121:230576
GI



I

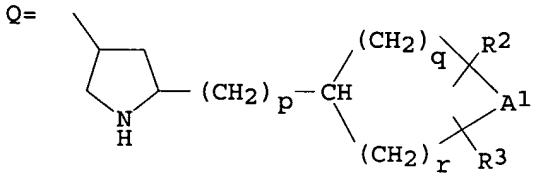
AB Title compds. I [R1 = (protected) carboxy; MeCH2OH, R4 = (substituted) pyridylalkyl, optionally N-substituted 2-oxopiperazin-1-ylalkyl, (substituted) imidazolalkyl, -pyrazolylalkyl, -triazolylalkyl, -pyrimidinylalkyl, -dihydropyrimidinylalkyl, -(2,3-dihydroimidazo[1,2-b]pyrazol-1-yl)ethyl; R5 = H, imino-protectant] or a salt thereof. To allyl (4R,5S,6S)-3-[(2R,4S)-1-allyloxycarbonyl-2-[2-(3-methyl-2-imidazolio)ethyl]pyrrolidin-4-yl]thio-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate iodide (preparation given), Ph3P, AcOH, and Pd(Ph3P)4 in THF/EtOH was added Bu3SnH to give the title compound (4R,5S,6S)-6-[(1R)-1-hydroxyethyl]-4-methyl-3-[(2R,4S)-2-[2-(3-methyl-1-imidazolio)ethyl]pyrrolidin-4-yl]thio-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid chloride (II). The min. inhibitory concentration of II in vitro against P. aeruginosa IAM1095 strain was

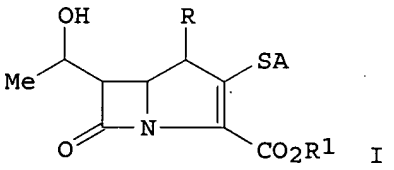
0.78 μg/mL.

L15 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:409028 HCAPLUS
DOCUMENT NUMBER: 121:9028
TITLE: Preparation of 2-(substituted pyrrolidinylthio)carbapenem derivatives as antibacterial agents
INVENTOR(S): Nakagawa, Susumu; Ootake, Kenichi; Nakano, Fumio; Yamada, Koji; Ushijima, Ryosuke; Murase, Satoshi; Fukatsu, Hiroshi
PATENT ASSIGNEE(S): Banyu Pharma Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 174 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

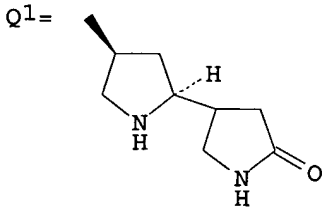
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05255330	A	19931005	JP 1991-263271	19910913

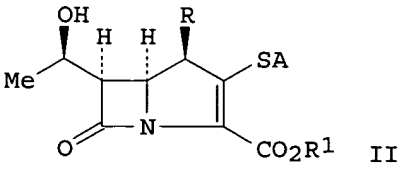
PRIORITY APPLN. INFO.: JP 1991-263271 19910913
OTHER SOURCE(S): MARPAT 121:9028
GI



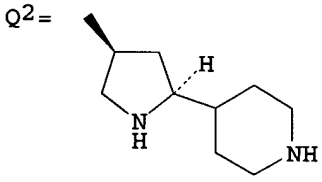


I





II



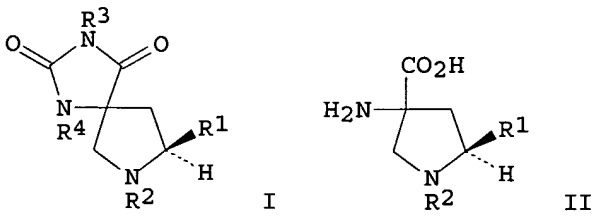
AB Title compds. [I; A = Q; R = H, Me; R1 = H, neg. charge; R2, R3 = H, lower (hydroxy)alkyl, formimidoyl, acetimidoyl, CO2R4, CONR5R6, NR5R6, CH2CO2R4, CH2NR5R6, CH2CONR5R6; R4 = H, lower alkyl; R5, R6 = H, lower alkyl; or NR5R6 forms aziridinyl, azetidinyl, pyrrolidinyl, piperidyl; A1 = NR7, N+R7R8, CONR7, CONR7CO, CONR7CONR8, NR7CO(CH2)s, NR8, NR7CO(CH2)sCOR8,

CONR7NR8, NR7(CH2)sNR8; R7, R8 = R2, R3; s = 1-3; p = 0-3; q, r = 0-5, q = p ≠ 0, q + p ≤6] are prepared I show potent antibacterial activity against antibiotic-sensitive and -resistant gram. neg. and gram pos. bacteria and excellent stability against β-lactamase and kidney dehydropeptidase I. Thus, p-nitrobenzyl (5R,6S)-2-diphenoxyphosphoryloxy-6-[(R)-1-hydroxyethyl]-1-carbapen-2-em-3-carboxylate was condensed with (2S,4S)-4-mercapto-N-(p-nitrobenzyloxycarbonyl)-2-(2-pyrrolidon-4-yl)pyrrolidine in the presence of (Me2CH)2NEt in MeCN at 0° to give, after hydrogenolysis over 10% Pd-C in a buffer solution of Na 3-morpholinopropanesulfonate, carbapenem derivative II (A = Q1, R = H, R1 = Na). II (A = Q2, R = Me, R1 = H) showed min. inhibitory concentration of 0.1, 0.39, and 1.56 μg/mL against Pseudomonas aeruginosa MB5000, MB5002, and β-lactamase-producing P. aeruginosa AKR17, resp. vs. 1.56, 3.13, and 6.25, resp., for imipenem.

L15 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:271177 HCAPLUS
DOCUMENT NUMBER: 120:271177
TITLE: Preparation of optically active amino acid derivatives having fixed conformation and anticonvulsants containing them
INVENTOR(S): Sawanishi, Hiroyuki; Myamoto, Kenichi; Tanaka, Kenichi; Suzuki, Koichi
PATENT ASSIGNEE(S): Tsumura & Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 40 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05213957	A	19930824	JP 1992-56058	19920207

PRIORITY APPLN. INFO.: JP 1992-56058 19920207
OTHER SOURCE(S): MARPAT 120:271177
GI



I II

AB The title compds. including spiropyrrolidineimidazoline derivs. (I; R1 = C1-6 alkyl, alkoxyalkyl, alkoxycarbonyl, hydroxyalkyl, CO2H; R2 = H, C1-6 alkyl, aryl, phenylalkyl, carbamoylalkyl, diphenylalkyl; R3, R4 = H, C1-6 alkyl, ester group) and aminopyrrolidinecarboxylic acid derivs. (II; R1, R2 = same as above), useful as anticonvulsants with low toxicity, are prepared Thus, ethylation of Me L-hydroxyprolinate with EtI in CH2Cl2 containing Et3N at 60° gave (2S,4R)-1-ethyl-4-hydroxy-2-methoxycarbonylpyrrolidine. Swern oxidation of the latter compound with

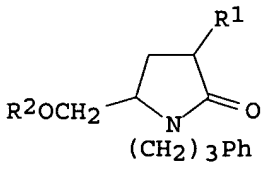
(COCl)2 and DMSO in CH2Cl2 containing Et3N at -60° gave (2S)-1-ethyl-4-oxo-2-methoxycarbonylpyrrolidine which underwent Bucherer-Bergs reaction with KCN and ammonium carbonate in 60% aqueous MeOH at 55-60° to give (3R,5S)-1-ethyl-5-methoxycarbonylspiro[pyrrolidine-3,5'-imidazoline]-2',4'-dione (III) and (3S,5S)-stereoisomer. A total of 65 I and II were prepared and 17 I in vitro inhibited 20-100% the carbachol-induced contraction of guinea pig's ileums. Seven formulations, e.g. 200 mg tablets containing 20 mg III, were described.

L15 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:539078 HCAPLUS
DOCUMENT NUMBER: 119:139078
TITLE: Preparation of 5-[(aminoaryloxy)methyl]-2-pyrrolidinoneacetates and analogs as drugs
INVENTOR(S): Himmelsbach, Frank; Austel, Volkhard; Pieper, Helmut; Eisert, Wolfgang; Mueller, Thomas; Weisenberger, Johannes; Linz, Guenter; Krueger, Gerd
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 173 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

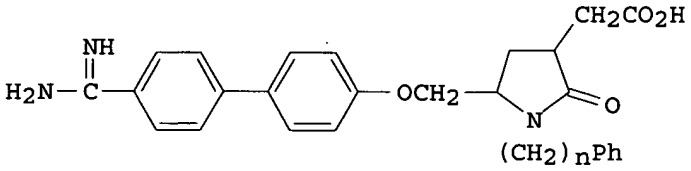
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 483667	A2	19920506	EP 1991-118148	19911024
EP 483667	A3	19920916		
EP 483667	B1	19980204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4035961	A1	19920507	DE 1990-4035961	19901102
AT 163008	T	19980215	AT 1991-118148	19911024
ES 2113867	T3	19980516	ES 1991-118148	19911024
SG 81852	A1	20010724	SG 1996-1241	19911024
FI 9105136	A	19920503	FI 1991-5136	19911031
FI 107606	B1	20010914		
CA 2054850	A1	19920503	CA 1991-2054850	19911101
CA 2054850	C	20010102		
NO 9104294	A	19920504	NO 1991-4294	19911101
NO 174806	B	19940405		
NO 174806	C	19940713		
AU 9186926	A	19920507	AU 1991-86926	19911101
AU 650488	B2	19940623		
JP 04264068	A	19920918	JP 1991-313154	19911101
JP 2937589	B2	19990823		
HU 67288	A2	19950328	HU 1991-3455	19911101
RU 2040519	C1	19950725	RU 1991-5001905	19911101
IL 99926	A	19960618	IL 1991-99926	19911101
KR 223135	B1	19991015	KR 1991-19458	19911102
ZA 9108734	A	19930504	ZA 1991-8734	19911104
US 5541343	A	19960730	US 1994-365336	19941228
US 5591769	A	19970107	US 1995-458096	19950601

PRIORITY APPLN. INFO.:
DE 1990-4035961 A 19901102
US 1991-783065 B1 19911025
US 1994-365336 A3 19941228

OTHER SOURCE(S): MARPAT 119:139078
GI



I



III

AB Compds. BXAYE [A = 4- to 7-membered (substituted) alkyleneiminodiyl; B = cyano, NO2, NH2, C(:NH)NH2, NHC(:NH)NH2, etc.; E = vinyl, CH2OH, cyano, SO2H, CO2H, alkoxycarbonyl, etc.; X = X5X4X3X2X1; X1 = bond, alkylene, or arylene which may be linked to X2 by O, SO2, CO, etc.; X2 = fluorenylene, arylene, hydronaphthaleneylene, etc.; X3, X5 = bond, (unsatd.) alkylene, etc.; X4 = bond, arylene, (bi)cycloalkylene; Y = Y1Y2Y3; Y1, Y2 = bond, (unsatd.) alkylene, etc.; Y3 = bond, arylene, alkylenearylene, etc.] were prepared Thus, (S)-5-[(trityloxy)methyl]-2-pyrrolidinone was condensed with Ph(CH2)3Br and the product alkylated with BrCH2CH:CH2 to give, after deprotection and mesylation, pyrrolidinone (3R,5S)-I (II; R1 = CH2CH:CH2, R2 = SO2Me) which was condensed with 4'-cyano-4-hydroxybiphenyl to give, after oxidation and esterification, II (R1 = CH2CO2Me, R2 = 4'-cyano-4-biphenylyl). The latter was converted in 2 steps to title compound (3R,5S)-III (IV; n = 3). IV (n = 0) had IC50 of 0.024 μM against binding of fibrinogen to human thrombocytes in vitro.

L15 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:7161 HCAPLUS
DOCUMENT NUMBER: 114:7161
TITLE: 4-Amino-3-alkylbutanoic acids as substrates for γ-aminobutyric acid aminotransferase
AUTHOR(S): Andruszkiewicz, Ryszard; Silverman, Richard B.
CORPORATE SOURCE: Dep. Chem., Northwestern Univ., Evanston, IL, 60208-3113, USA
SOURCE: Journal of Biological Chemistry (1990), 265(36), 22288-91
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A variety of alkyl-substituted 4-aminobutanoic acid derivs. H2NCH2CHRCH2CO2H [R = (RS)-Me, -Et, -Pr, -CHMe2, -Bu, -CH2CHMe2, -CHMeEt, -CMe3; (R)- and (S)-Me, -Et], H2NCH2CMe2CH6CO2H, (E)-H2NCH2CMe:CHCO2H, and (R)-, (S)-, and (RS)-H2NCHMeCH2CH2CO2H were synthesized and tested as alternate substrates for purified γ-aminobutyric acid aminotransferase (EC 2.6.1.19) from pig brain. All of the compds. were substrates, but their activities diminished as the size and bulk of the 3-alkyl substituent increased. Several differences were observed between the alkyl-substituted analogs and the corresponding aryl-substituted compds. previously reported (Silverman, R. B.; et al, 1987). These findings will be important in future designs of inhibitors of γ-aminobutyric acid aminotransferase.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	310.47	680.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-50.70	-50.70

STN INTERNATIONAL LOGOFF AT 11:59:20 ON 01 MAR 2007